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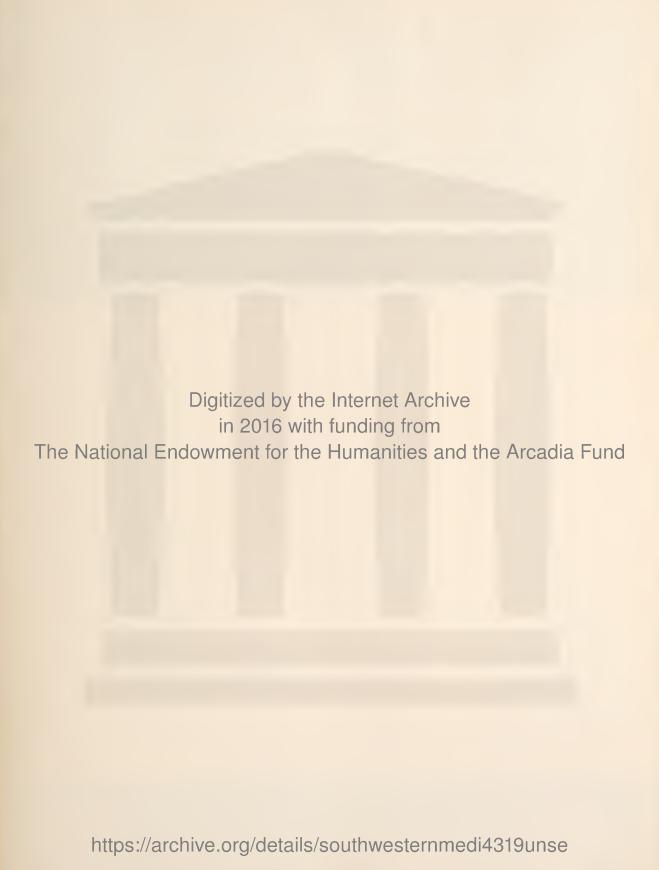
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# Southwestern MEDICINE

Official Journal of The Southwestern Medical Association,
The Western Association of Railway Surgeons, The Southwest Obstetrical and Gynecological Society,
Southwestern Dermatological Society, Texas District One Medical Association,
The Southwestern New Mexico Medical Society, and El Paso County Medical Society

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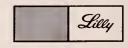
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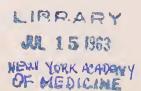
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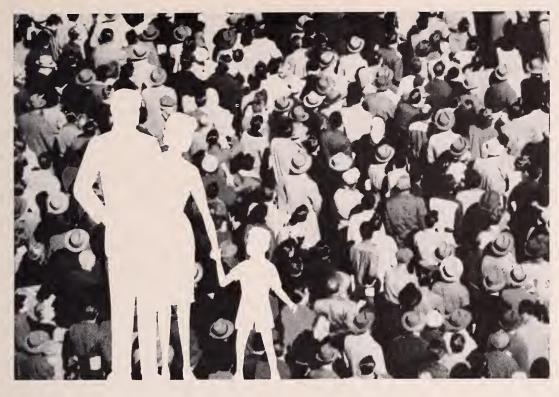
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VOL. 43 JANUARY, 1962 NO. 1

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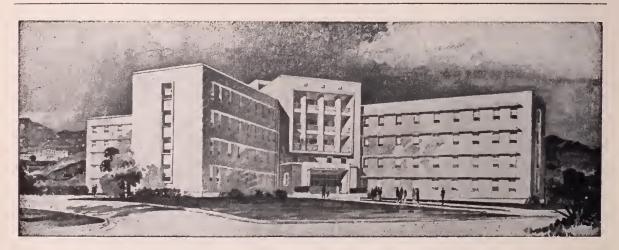
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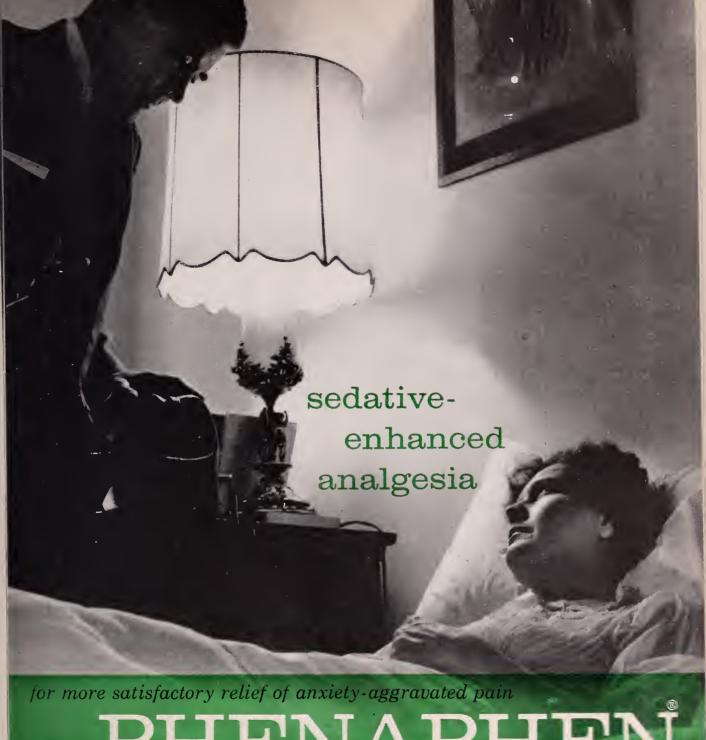
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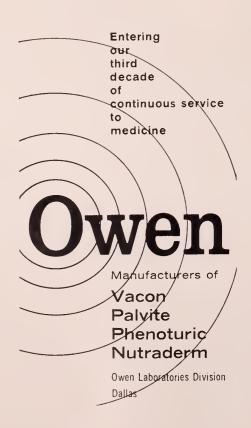
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#### Coming Meetings

University of Texas Postgraduate School of Medicine. El Paso Division, Postgraduate Course, El Paso County Medical Society Turner Home, 1301 Montana Avenue. Jan. 21. 1962.

International Medical Assembly of Southwest Texas, 26th Annual Session, Granada Hotel, San Antonio, Jan. 29-31, 1962.

District One, Texas Medical Association, Annual Meeting, Pecos Country Club, Pecos, Texas, Feb. 3, 1962.

American College of Allergists, Graduate In-

structional Course and 18th Annual Congress, Hotel Radisson, Minneapolis, April 1-6, 1962.

The Western Association of Railway Surgeons, annual meeting, Stockmen's Motor Hotel, Elko. Nev., Sept. 27-29, 1962.

Southwest Obstetrical and Gynecological Society, 12th Annual Meeting, Camelback Inn, Phoenix, Oct. 10-13, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.



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# MEETINGS

Dr. Stowe

Elected President

# of El Paso County Medical Society

Dr. Jesson L. Stowe has been elected president of El Paso County Medical Society for the 1961-62 year. He succeeds Dr. Louis W. Breck.

Other new officers are Dr. W. R. Gaddis, President-Elect; Dr. H. D. Garrett, Vice-President; Dr. Carlos A. Fernandez, Secretary; Dr. Wayne Lorentzen, Secretary-Elect; and Dr. Charles Green. Treasurer.

Born in Midland, Texas, Dr. Stowe is a graduate of El Paso High School and received his B.A. from Baylor University and his M.D. from Baylor University College of Medicine.

He interned in El Paso-City-County Hospital, now Thomason General Hospital, and St. Paul's Hospital in Dallas. He did two years of post-graduate work at Philadelphia Lying in Unit, Pennsylvania Hospital, and University of Georgia Medical College. He has practiced medicine in El Paso since 1932.

He is a Past President of the Texas Association of Obstetricians and Gynecologists and a member of the association's executive committee.



Dr. Stowe

A former Chief of Staff for Southwestern General Hospital in El Paso, he is at present chief of the hospital's Obstetrics and Gynecology service. From 1935 until 1950 he was Chief of Staff at the Newark Maternity Hospital in El Paso. He is a former chief of obstetrics and gynecology service at Thomason General Hospital.

Dr. Stowe is a former council member of the Southwest Obstetrical and Gynecological Society and a member of the Central Association of Obstetricians and Gynecologists and the American College of Obstetricians and Gynecologists.

Dr. and Mrs. Stowe reside at 624 E. College Ave, with their sons, James L., 11, and Robert H., 9. Dr. Stowe has a daughter, Mrs. Kenneth Boll, in Fort Leavenworth, Kan.

# TMA President to Speak at District One Meeting in Pecos

Annual meeting of District One of the Texas Medical Association will be held Feb. 3 in Pecos.

The meeting will hear a luncheon talk by Dr. Harvey Renger of Hallettsville, President of the Texas Medical Association.

Officers of the District One Association are Dr. Harold Lindley, Pecos, President; Dr. E. S. Crossett, El Paso, Vice-President; Dr. Gordon L. Black. El Paso, Secretary-Treasurer; Dr. William Gaddis. El Paso, Secretary-elect; and Dr. Charles Oswalt, Fort Stockton, counselor.

The complete program follows:

9:00- 9:30 a.m. Surgical Treatment of Duodenal Ulcer

J. O. Dampeer, M.D., Kermit, Texas

9:30-10:00 a.m. Thoracic Surgical Problems in Infancy

E. O. Crossett, M.D., El Paso

10:00-10:15 a.m. Coffee

10:15-10:45 a.m. Management of Patient with

Abnormal Pap Smears James Morgan, M.D., El Paso

10:45-12:00 noon Terminal Care of Pelvic Cancer Joseph Lucci, M.D., Houston

12:00- 2:00 p.m. Luncheon
Guest Speaker, Harvey Renger,
M.D.

2:00- 2:30 p.m. Use of Radio-Active Isotopes in Clinical Diagnosis
M. S. Hart, M.D., El Paso

2:30- 3:00 p.m. Management of Pulmonary Emphysema Edward Downs, M.D., El Paso

3:00- 3:15 p.m. Coffee

3:15- 4:00 p.m. Treatment of Rattlesnake Bite Charles Oswalt, M.D., Fort Stockton

Four and one-half hours Category II credit will be given by the American Academy of General Practice.

Ladies program to be announced.

### Session in Psychiatry Scheduled in Phoenix

"Psychiatry in the Practice of Medicine" will be the subject of a two day seminar Feb. 3 and 4 at the Ramada Inn in Phoenix.

The seminar is being jointly sponsored by the University of Southern California school of medicine's department of psychiatry and medicine, and the Arizona Academy of General Practice.

The faculty of the University of Southern California will furnish the teaching personnel.

Principal speakers will be Edward Stainbrook, M.D., Professor of Psychiatry, chairman of the department of psychiatry, University of Southern California; and Allen J. Enelow, M.D., Associate Clinical Professor, department of psychiatry, University of Southern California.

Category I credit of 10 hours will be given for this course.

Inquiries should be addressed to Allen J. Enelow, M.D., Associate Clinical Professor, department of psychiatry, 1934 Hospital Place, Los Angeles 33, California.

James L. Grobe, M.D., is chairman of mental health for the Arizona Academy of General Practice.

# AAGP Meeting in Las Vegas, N. M.

Diagnosis and treatment of psychiatric cases will be discussed at a two-day postgraduate meeting of the New Mexico Chapter of the American Academy of General Practice to be held in Las Vegas, N. M., March 9 and 10, 1962, Dr. Leland S. Evans, Las Cruces, Regional Advisor for the AAGP's Commission on Education, has announced.

Scientific meetings on Friday, March 9, will be conducted at New Mexico State Hospital, and on Saturday, March 10, at Highlands University.

The complete program follows:

#### Friday, March 9

#### Morning Session

Roy Robertson, M.D., Albuquerque, Presiding

9:00- 9:30 Registration

9:30- 9:45 Welcome Address

Thomas Hogshead, M.D., Las
Vegas

9:45-10:30 Experiences by WICHE in Psychiatric Refresher Courses.

Warren Vaughan, Jr., M. D., San Mateo, Calif.

10:30-11:15 Future Programs and Goals in Care of Emotionally Disturbed Patients.
Robert Hewitt, M.D., Boulder,
Colo., Director, WICHE

11:15-11:30 Recess

11:30-12:15 Experiences in Teaching Non-Psychiatrist Physicians.

Theodore Watters, M.D., New Orleans

12:15 Luncheon

#### Afternoon Session

C. Pardue Bunch, M. D., Artesia, N.M., Presiding

2:00- 2:45 Office Treatment of Emotional Illness by the Family Physician.

William Sheeley, M.D., Washington, D. C.

2:45- 3:30 Panel Discussion

Drs. Vaughan, Hewitt, Watters, Sheeley, Robertson, and Bunch.

3:30- 3:45 Recess

**3:45- 4:30** The Doctor, His Family, and Psychiatry.

Theodore Watters, N.M.

#### Saturday, March 10

#### Morning Session

Thomas Hogshead, M.D., Las Vegas, Presiding

9:00- 9:40 Teamwork Between Psychiatric and Non-Psychiatric Physicians. Warren Vaughan, Jr., M.D.

9:40-10:10 Going Home for Keeps. William Sheeley, M.D.

10:10-10:40 Planning for Better Mental Aftercare. Robert Hewitt, M.D.

10:40-11:00 Recess

11:00-12:00 Panel Discussion.

Drs. Vaughan, Sheeley, Hewitt, and Hogshead

12:15 Luncheon

#### Afternoon Session

#### William Sears, M.D., Los Alamos, N.M., Presiding

2:00- 2:45 Psychological Examinations of Patients.

Stuart Boyd, Ph.D., Head of Psy-

chology Department, Highlands University

University

2:45- 3:30 Coordinating Mental Health Programs with the Medical Profession.

Lester Libo, Ph.D., State Health

Department, Santa Fe

3:30- 3:45 Recess

3:45- 4:30 Panel Discussion.

Drs. Libo, Boyd, and Sears. Moderator: Dr. Leland S. Evans.

This program is made possible by a grant from Eli Lilly and Company.

# Writing Awards Contest Rules Are Revised

Rules for \$500 in writing awards in contest being conducted by *Southwestern Medicine* for the best original scientific articles to be published in *Southwestern Medicine* starting with the January, 1962, issue follow:

The contest for the first year, 1962, will close on Sept. 1, 1962, so that judging can be completed and awards made at the 44th annual meeting of the Southwestern Medical Association in Albuquerque, N. M., Oct. 18-20, 1962. From that date, the contest will run from Sept. 1 to Sept. 1 of each year.

The awards will be made in two classifications: Regional and National. All physicians who practice in West Texas, Arizona, New Mexico, Nevada or Northern Mexico (States of Sonora and Chihuahua) will be eligible to compete for the Regional Awards. All physicians in the United States outside the Regional area may compete for the National Awards.

Only original scientific articles published in Southwestern Medicine will be eligible.

Awards will be made in the following amounts for the best original articles written by physicians in the Regional Area: One Hundred (\$100.00) Dollars for the best paper. Seventy-Five (\$75.00)

Dollars for the second best paper. Fifty (\$50.00 Dollars for the third best paper.

Awards for the best original articles written by physicians in the National classification (outside the Regional Area) will be made in the following amounts: One Hundred (\$100.00) Dollars for the best paper. Seventy-Five (\$75.00) Dollars for the second best paper, Fifty (\$50.00) Dollars for the third best paper.

An additional Fifty (\$50.00) Dollars will be set aside annually to establish a fund for a special classification to be known as the Intern and Resident Writing Awards. Original scientific articles submitted by resident physicians and interns of the Regional Area will be eligible for special awards to be announced at a future date.

Contributions must be written in English. They must be typed, double spaced and on one side of paper only. A stamped, self-addressed envelope must be included with each paper to insure return of rejected manuscripts.

All papers should be submitted to Lester C. Feener, M.D., Editor, 310 North Stanton Street, El Paso, Texas. As with all official medical journals, only those papers found acceptable by the board of editors of the journal will be published.

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# Viral Respiratory Diseases In Southwestern Indians Serological Evidence

WILLIAM E. CLAPPER, Ph.D., Albuquerque Conrad Ellner, M. D., San Francisco Maxine C. May, M. T., Winslow, Arizona John C. Cobb, M. D., Baltimore

About 20 per cent of the non-bacterial respiratory diseases are caused by viral and rickettsial agents. Influenza, parainfluenza, psittacosis, respiratory syncytial, adenovirus, and Q fever rickettsiae are involved in many epidemics of these diseases. Since all such infections are not severe or of epidemic proportions, it is often possible to determine their prevalence only by determining the antibody level in a selected group of the population.

To discover whether several of these diseases were as common in a comparatively closed group as in other segments of the population, serum complement fixing (CF) antibody titres were studied in two groups of Southwestern Indians. The larger number of serums were obtained from Indians of the Taos Pueblo, New Mexico, and the smaller sample, obtained entirely from children, was taken at the boarding school in Chinle, Arizona.

Influenza A and B, adenovirus, and Q fever, CF antibodies and cold agglutinins, were determined on serum collected from 182 individuals. Parainfluenza CF titres were also done on the Chinle group. Psittacosis was not included because it was thought that opportunity for exposure was small and that significant results would be unlikely.

#### Methods

Complement fixing antibody titres were deter-

mined by the method described by Jensen.<sup>2</sup> Antigens and antisera for influenza B, Q fever, and psittacosis were obtained from Markham Laboratories and Lederle Laboratories. Influenza A antigen (Japan/305/57) was kindly supplied by Dr. R. Q. Robinson of the Communicable Disease Center, Montgomery, Alabama, and postive serum for control of the cold agglutinin test by Dr. Edwin Lennette of the State of California Department of Public Health.

The antigen and antiserum for adenovirus were purchased from Microbiological Associates. The adenovirus antigen was later made in our own laboratory from a type 4 strain supplied through the courtesy of Dr. Gordon Meikeljohn of the University of Colorado Medical School. Box titrations were performed to determine the optimal concentration of antigen to use. Titres were determined after overnight incubation at 4°C.

#### Taos Group

Serums from the Taos group were taken from most of those presenting themselves for any kind of medical care during the fall and early winter months of 1958-59. When possible, second specimens from the same individuals were taken during the spring months to determine whether a rise in titre had occurred. Table 1 shows the results of a study of 42 paired serums taken from patients

aged 12 to 82 years. Of these, 20 complained of upper respiratory symptoms at some time during the winter.

TABLE 1

Incidence of Viral Respiratory Disease 1958-59

Taos Indian Group

Total Paired Specimens 42	Influenza A	Influenza B	Adeno- virus	Q fever	Cold Ag- glutinins
Two-fold rise	9	12	31	2	2
Four-fold rise	5	7	19	0	0

First specimens taken two to six months before second

Only two showed serologic evidence of infection with influenza A and three with influenza B virus. No four-fold rises in titre were observed in any of the 42 for Q fever complement fixing antibodies or for cold agglutinins. Perhaps this could be expected, as cold agglutinins are usually absent four to six weeks after onset of symptoms.<sup>3</sup>

The finding that 19 per cent of this group had a four-fold rise in adenovirus CF titre may be of significance. Price<sup>4</sup> believed that determining titres at four-month intervals would identify adenovirus disease, since the titre remained elevated for at least four months. He found that only four per cent of students studied over a two-year period showed evidence of having been infected with one of these viruses.

Grayston and his co-workers<sup>5</sup> reported a random; serological survey from Army recruits in which 16 per cent were positive by CF test. Jordan<sup>6</sup> states that 0.5 to three per cent of unselected hospital patients with respiratory symptoms were found to be infected with an adenovirus. Our results in members of an isolated group suggest that their experience with this virus may be more nearly like that reported in studies of recruits than like those of urban populations in our country.

Information concerning the length of time CF antibodies persist was elicited from studies of titres taken at different time intervals. Seven showed a four-fold decrease in influenza B titre within three to six months. Three of these showed eight-fold decreases in three months; three 1-16 titres to

adenovirus were found to be negative six months later.

No drop in titre was seen in two patients in one month, but both were negative three and four months after the initial titre was found to be 1-16 and 1-32, respectively. Apparently, if no antigenic stimulus, either homologous or heterologous is received, the antibody responses to these two viruses may disappear completely in four to six months.

The titres found in 123 specimens of serum from members of the Taos Pueblo are shown in Column A of Table 2. For comparative purposes, titres for the Chinle Indian children and a group of varying ages seen at the Lovelace Clinic in Albuquerque, during the same period, are included in the table. Twenty-six of the clinic group were healthy men having a routine physical examination. The titres on the Taos group indicate only that a large proportion were probably exposed to influenza B and adenoviruses during the winter and a smaller proportion to influenza A.

They had not been given influenza or adenovirus vaccine. The level of cold agglutinins was similar to that of the CF antibodies for influenza A. The cold agglutinin titres were in agreement with the statement of Feller and Hilleman<sup>3</sup> that 1-32 or 64 would be considered abnormal.

It was expected that evidence for Q fever might be found because of the somewhat primitive conditions under which the group lives and its possible frequent contact with cattle and goats. Although only four per cent of the 123 examined showed a titre of 1-8 or greater, this compares in significance to that found in a survey made in Utah in which the highest percentage of positives found was in one county with 7.7 per cent.<sup>7</sup>

This may also be compared to 41 clinic patients whose serums were examined for Q fever complement-fixing antibodies in which only one 1-8 titre was found. This indicates the presence of the disease, and further serological studies of larger numbers taken from other population segments might uncover an appreciable amount of infection in the state.

#### Chinle, Arizona Group

A respiratory epidemic involving 26 Indian children (ages 8-12) in the Pinon Boarding School came to our attention in December, 1958. The

medical officer in charge sent serums for CF tests and described the illness as being characterized by temperatures of 100° to 103°F, for three to seven days with a non-productive cough and rales varying from fine to coarse. There was no associated pharyngitis, lymph adenopathy, splenomegaly, myalgia, or arthralgia. An x-ray of the chest was obtained on one patient only and this was negative. Throat cultures taken by the medical officer were reported to have shown normal flora.

Four children received penicillin; the remaining 22 had aspirin and bed rest. All but one recovered within a week. The serum specimens in the acute phase were taken about ten days after symptoms first appeared and in the convalescent phase about two weeks after the acute. Twelve paired speciments were received and six with the acute specimen only.

There were no four-fold rises in CF titres against influenza A, influenza B, adenovirus, or Q fever nor in cold agglutinin titres. The two specimens showed the same titre in almost every case. This may have been due to the first having been taken after the acute phase, although the second specimen might be expected to show a higher titre if any of the antigens used were those causing the epidemic.

However, it is interesting to compare the titres of these serums which are given in Column B of

Table 2

Comparative Titres for Respiratory Disease in Three Groups

	Complement fixing				Cold ag-	
Titres	Influenza A	Influenza B	Adeno- virus	Q fever	PAP*	
	A B C	A B C	A B C	A B C	A B C	
	in per cent					
1-8 or greater	21 17 37	70 33 84	86 94 89	4 0 1	28 61 19	
1-16 or greater	2 0 5	69 33 67	63 94 52	1 0 0	11 22 2	
1-32 or greater 1-64 or	0 0 0	36 0 31	32 89 40	0 0 0	3 17 2	
greater 1-128 or	0 0 0	8 0 10	6 39 17	0 0 0	2 5 2	
greater	0 0 0	0 0 3	1 5 2	0 0 0	0 0 0	

\*PAP = Primary Atypical Pneumonia

A — Taos group, 123 subjects

B — Chinle group, 18 subjects

C - Clinic group, 41 subjects

Table 2 with those of the Taos group in Column A and the clinic group in Column C. There was no evidence of Q fever in the Chinle group. The titres for influenza A were about the same as for the Taos group, but were lower for influenza B. Those for adenovirus were remarkably higher, as were those for cold agglutinins.

If the epidemic was not caused by an adenovirus, exposure to this organism must have been in the recent past. No vaccine for any of the agents had been given previously. The higher titre for cold agglutinins might be explained on a similar basis, or since this is a non-specific reaction, it might have been due to some other common factor in this group not related to primary atypical pneumonia. Eight paired serums were also examined for CF antibodies to parainfluenzae 1 and 3 since the symptoms were not unlike those described by Parrott *et al.*<sup>8</sup> for these viruses. No four-fold rises in titre were observed. All had titres of 1-8 or 1-16 for parainfluenza 3, but only one had a titre of 1-8 for parainfluenza 1.

Similar results were found on 19 additional children in the Albuquerque area, ranging in age from two to 15 years. Titres for all five of the respiratory diseases studied in the clinic group are quite similar to those of the Taos group. The higher titres to adenovirus in the Chinle group might be explained by the fact that this group was composed entirely of children while the other two groups were mostly adults. Jordan<sup>8</sup> states that 50 per cent of children have adenovirus CF antibodies at the age of 10 years and Balducini et al.<sup>9</sup> found CF antibodies mainly in persons under 30 years of age in England. The 94 per cent found in the Chinle children is still considerably higher than these figures.

#### Summary

Serologic evidence was found in a selected group of the Taos Indians for the presence of influenzae A and B, adenoviruses, Q fever rickettsiae, and the primary atypical pneumonia virus giving rise to cold agglutinins. Influenza B and adenovirus infections were most prevalent during the winter of 1958-59. The infection rate with adenovirus was much higher than has been observed in urban populations. A low incidence of Q fever antibodies was found.

CF antibodies to influenza B and adenovirus were found to disappear in three to six months when the initial level was 1-32 or less.

A group of Arizona Indian children involved in a respiratory epidemic showed less evidence of exposure to influenzae A and B, but nearly 100 per cent had titres to adenovirus with the average titre higher than was found in the other two groups.

The Arizona Indian children showed serologic evidence of a high exposure to parainfluenza 3 and low to parainfluenza 1. The causative agent of the epidemic was not proved to be due to any of the six agents for which tests were carried out.

#### Acknowledgments

We are indebted to Dr. Albert C. Diddams, Field Medical Officer in Charge, Chinle Health Center, Chinle, Arizona, for sending serums from children with respiratory disease for study.

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# Blue Cross Undertakes Portion of Medical Care Program

Jan. 1, 1962, is a significant date for approximately 221,000 Texas Old Age Assistance recipients who will become eligible for certain types of medical care within the provisions of the Kerr-Mills Act. The program is state-operated and controlled even though federal funds are provided. The federal act was implemented in Texas by the Medical Assistance Act.

The program is twofold and includes funds for (1) inpatient care in the hospital, including medical and surgical services performed by physicians, and (2) nursing home care. Blue Cross of Texas will underwrite the first portion of the program. The State Department of Public Welfare will administer the nursing home phase, which is not an insured program.

The Texas State Department of Public Welfare is chief administrator of the program. After extensive investigations, the Department accepted a plan submitted by Blue Cross of Texas as the "most practical and efficient method of handling the

hospital-doctor phase of the program".

Individual physicians must certify patients who are to receive benefits from the program. Hospitals will be responsible for obtaining certification of a patient's eligibility from the State Department of Public Welfare. The forms, which are to be kept by the hospital and not by the individual physician, contain a clause for the physician's certification that the patient is acutely in need of medical care provided for under the provisions of the program. At the end of 15 days hospitalization, the doctor must recertify the patient if continued care is necessary. Again, the hospital must secure certification from the Department that the patient still is entitled to Old Age Assistance.

In January the Department will mail each Old Age Assistance recipient an IBM card from Blue Cross containing his name and a number assigned to him by the State Department of Public Welfare. In case the patient requires medical care, he is to show this card to the physician and to the hospital.

### Abdominal Pain and Shock in Hemochromatosis

#### A Possible Explanation

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Idiopathic hemochromatosis was first described by Hartman and Chousser<sup>28</sup> in 1882. They described the classical tetrad of liver diseases, diabetes, pigmentation and atrophy of the gonads. Howard and Stevens<sup>28</sup> in 1917 were among the first to demonstrate that abnormal iron metabolism was the bases of this condition.

This is not a common condition. Sheldon<sup>2</sup> was able to find only 345 cases described until 1935. The disease is probably genetically determined.<sup>7,8</sup> One-half to one-third of siblings of patients with idiopathic hemochromatosis have increased iron absorption when measured by radio-active iron techniques.<sup>8</sup>

In hemochromatosis, there appears to be excess iron absorption from infancy and childhood: The body excretes less than one mgm of iron daily in the bile and small amounts in the sweat. Although absorption of iron may not be much increased over normal each day, as the years pass, massive deposits of iron are accumulated. Sheldon<sup>2</sup> estimated that it needed about 28 years for the disease to become manifested in the average case.

The iron is stored as ferratin, which is a combination of iron and apoferratin, and hemosiderin, which appears to be aggregated ferratin molecules. The parenchymal distribution is that seen in oral iron overload. These iron stores may be mobilized by repeated phlebotomy. While the fundamental defect appears to reside in the mucosal cell of the

gastro-intestinal tract,<sup>23</sup> there is evidence that there may be a defect in the reticulo-endothelial system.

Iron given intravenously is picked up by the reticulo-endothelial system. Large amounts of oral iron are picked up by the parenchyma and the reticulo-endothelial system. In idiopathic hemochromatosis the iron is picked up primarily by the parenchyma and little by the reticulo-endothelial system. This suggests there may be defect in the ability of this system to remove iron.

The average patient with hemochromatosis dies of various complications of his illness. Before the advent of insulin the majority died as a result of the associated diabetes. Now however, they die usually as a result of cardiac decompensation or the end results of liver disease; ie, hepatic coma, hepatoma or bleeding esophageal varices.

Recently there have been increasing reports of patients with iron storage disease, who develop severe abdominal pains, shock, and die as a result of this sudden calamity. The authors wish to describe a patient in this latter group.

#### Case Report

A 45 year old female was first seen in consultation on 10/17/60, because of bronzed skin and diabetes. There was no family history of diabetes or bronze skin. Past history revealed that the patient had been discovered to have "anemia" and an enlarged spleen in 1950. She had received nu-

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merous blood transfusions and had been splenectomized at that time for "hemolytic anemia," type not specified. The records could not be obtained from the hospital where this procedure took place. In 1951, the patient had a cholecystectomy allegedly for "gall stones."

Eight years ago the patient noted that her skin was becoming darker. For six months she noted polydipsia and polyuria. She had lost 16 pounds in weight. For three months she had noticed persistent right upper quadrant pain. The patient sought medical care from her family physician, who suspected that she had hemochromatosis and hospitalized her in the Flagstaff Hospital.

Physical examination revealed a thin female with gray dry hard skin. Temperature 99, pulse 110, respirations 26, blood pressure 118/70. Head and neck, no abnormality noted; heart, not enlarged, no thrills or murmurs; lungs, clear to percussion and auscultation. Abdomen, liver enlarged three fingers below costal margin; it felt very firm. Scars present in right and left upper quadrants from previous surgery. No spider angiomata, Extremities normal.

Laboratory findings: Hb. 14.5, RBC 5.4 million, WBC 10,800, P. 70 L. 26 E. 4; Urine-spec. grav. 1035, Alb neg, sugar 4+, Mic.-neg. Blood sugar—274 mgm, total protein—6.55 Gms. alb—5.50 Gms, glob—1.05 Gms, cholesterol—138 mgm, thymol turb—5.6 mgm, ceph. floc—3+, Kahn—neg, EKG—normal, chest X-ray—normal. Liver biopsy—"Fibrosis of liver and iron deposits in keeping with hemosideroses and probable hemochromatosis."

#### Course

The patient was treated with 2500 calorie diet. 35 units Lente insulin (U-80). This controlled her diabetes. She received five phlebotomies of 500cc each which reduced her hemoglobin to nine grams.

The patient was discharged from the hospital and was followed in the office. Her diabetes remained under good control, but phlebotomies were eventually discontinued, because the condition of her skin made it almost impossible to enter a vein.

On 2/1/61, the patient noted facial and ankle edema. This steadily progressed and was asso-

ciated with breathlessness and ascites. The patient was readmitted to the hospital 2/8/61. Examination was similar to that of 10/17/60, save for facial edema, ankle edema and ascites.

Examination of the heart revealed a presystolic gallop rhythm. EKG revealed diffuse T wave inversions, which were not present on the previous tracing. Chest roentgenogram evidenced marked increase in the heart size. The patient was placed on a 2500 calorie low salt diet, digitoxin, chlorothiazide and her insulin requirement remained the same. She was discharged, edema free, on 2/14/61.

On 2/25/61, the patient suddenly developed severe epigastric and right upper quadrant pain, which radiated into the back. The patient became weak, sweaty and vomited. She was examined at home, and found to have no pulse or blood pressure. She was admitted to the Flagstaff Hospital, where the pertinent physical findings were the absence of pulse and blood pressure and diffuse upper abdominal tenderness. Rigidity and rebound were not present.

**Laboratory findings:** Hb. 12, RBC 4.6 million, WBC 16,100, P. 72, L. 18.

Catheterization of bladder—no urine present. Amylase 12, Somoygi Units, Na. 130, K. 5.8, Urea 120, EKG-diffuse T waves inversions, first degree heart block.

#### Course

The patient received sedation, "Cedalinid" 4mgm IV, 100 mgm Prednisone intravenously, an infusion of 1000cc five per cent glucose and water with eight ampoules of Levaphed in it and 500cc of blood. Despite therapy her pulse and blood pressure were never obtainable and she died four hours after admission.

#### Post Mortem Findings

Autopsy revealed a strikingly wasted and cachectic middle aged white female. The most conspicuous feature was the uniform, dark brown color of the skin. The abdomen showed several old surgical scars. The myocardium was a golden brown color. The lungs were edematous. The spleen was surgically absent.

The markedly enlarged liver showed abundant adhesions over the surface. It's cut surface was dark brown, finely nodular, such nodules being 2-3 mm in size, separated by zones of dense fibrous tissue.

Gallbladder was absent. The left adrenal was very small. The right was enlarged. It contained two fairly discrete nodules of tissue resembling cortex each about one cm. in size. The pancreas was small in size, firm and fibrous and of a dark brown color. The lymph nodes generally were slightly enlarged, soft and dark brown in color.

Microscopically, extremely abundant brown pigment was seen in the pancreas, liver, lymph nodes, heart and adrenals and lesser amounts elsewhere. The pigment was demonstrated to be predominately iron by the Prussian blue reaction. In the pancreas there was extreme diffuse fibrosis. Loss of exocrine parenchyma was extreme. Islets were better preserved.

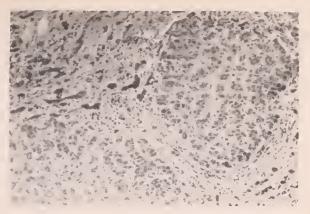
The liver showed severe portal fibrosis, bile duct proliferation and lymphocytic infiltration associated with the pigmentation. It is of interest that the pigmentation in the adrenals was limited to the most superficial zone at the cortex. In the kidney, some tubules appeared atrophic, with small pigment containing epithelial cells.

#### Discussion

This patient suddenly developed an acute medical calamity, the cause of which could not be



Pancreas. The most conspicuous features are heavy pigmentation and extreme fibrosis. Loss of exocrine parenchyma is more marked than loss of islets. Pigment is demonstrated in parenchymal cells and islet cells as well as interstitial fibrous tissue.



Liver. The parenchyma consists of small, irregular, highly variable-sized nodules of hepatic cells separated by broad zones of fibrous tissue containing abundant proliferating bile ducts and moderate lymphocytic infiltration. Pigment within the fibrous zones is abundant. Pigment is also present in both hepatic parenchymal cells and in Kuppfer cells.



Adrenals. In both adrenals the zona glomerulosa is narrowed, but is rendered of increased prominence by reason of an abundant deposition of brown, fairly granular pigment. This is not seen elsewhere in the glands.

immediately determined. The patient failed to respond to the usual medications employed for treating shock. Autopsy failed to give a ready explanation for the patient's sudden demise.

The authors early entertained the idea that the patient might have developed acute adrenal insufficiency. The patient's sodium was low, her potassium was elevated as was her urea. The occurrence of adrenal insufficiency associated with hemochroniatosis has been reported in the past. Rogers<sup>14</sup> and Wood<sup>15</sup> have reported cases of adrenal insufficiency secondary to hypopituitarism associated with hemochromatosis.

In these cases, there was marked replacement of pituitary gland by iron pigment and fibrous tissue. Against this explanation for the patient's shock is the absolute lack of response to large doses of steroids. Also the electrolyte difficulties manifested by this patient may often be seen in severe shock states from any cause.

Severe abdominal pain and shock in far advanced hemochromatoses, has been reported with increasing frequency. Sheldon<sup>2</sup> demonstrated that six per cent of patients with hemochromatosis had severe abdominal pain. Deforges<sup>17</sup> reported on six patients who had severe abdominal pain associated with their iron storage disease. In three cases he assigned the cause to liver failure, diverticulitis and hepatoma. In three cases the cause for the pain was not determined. Two of these latter patients also manifested shock. He quotes Boulin<sup>19</sup>, who stated that 34 per cent of his patients with hemochromatosis evidenced severe abdominal pain.

Boland and Curran<sup>18</sup> reported on two brothers with iron storage disease and severe abdominal pain. They operated on one brother and found no cause for his pain other than hemochromatosis.

McClatchie, et al<sup>16</sup> reported on a patient with iron storage disease and pain on whom they operated. No cause for the pain was discovered and the patient died in hepatic coma. These authors postulated that a sudden release of ferratin into the circulation might account for the symptoms. Mazur and Shorr <sup>21</sup> have identified vaso-depressor material (VDM) as being identical with ferratin. VDM, they feel, is released in shock and causes the irreversable shock state. It has been shown that excess iron is stored in the liver as ferratin as well as hemosiderin. McClatchie et al<sup>16</sup> were unable to demonstrate any adrenal disease in their patient.

Taylor<sup>20</sup> presented two patients with abdominal pain and hemochromatosis. He felt that the tissues were saturated with hemosiderin and ferratin. Sudden release of large amounts of ferratin, he suggested, gave rise to abdominal pain and shock. The liver of one patient at autopsy assayed for ferratin content, revealed .18 ml per gram of tissue with a normal of about .067 ml per gram.

Livingston<sup>26</sup> reported a similar case which he attributed to excess ferratin in the circulation. Gloor<sup>27</sup> reported another similar case in 1956.

The authors feel that the hypothesis of "acute ferratin intoxication" best explains what happens to these patients. It also implies that these patients carry with them the instrument of their own destruction. If the patient escapes death from cardiac or liver disease he may succumb to sudden release of ferratin into his circulation.

#### Summary

A case of abdominal pain and shock associated with hemochromatosis has been presented. The literature has been briefly reviewed. The authors feel that the hypothesis of sudden release of large amounts of ferratin into the circulation best explains the syndrome of abdominal pain and severe shock seen in this patient.

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# Trial With an Anabolic Agent in a General Practice

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It was decided to try an anabolic agent |oxymetholone\*) in a general practice on a variety of patients. The only criteria necessary to determine which patients would qualify for a trial on this drug were that he or she were below their standard weight and that all previous measures to put on weight had failed. Twenty-five patients were so followed.

#### Method

This was simply to give the patients the drug in tablet form which were supplied in 2.5 mgr. strengths. Patients aged 3-15 were given 2.5 mgr./day, those 15-20 were given 2.5 mgr. twice a day

and those over 20 were given 2.5 mgr. three times a day. The patients then were followed bi-monthly with weight measurements as well as arm, thigh and girth measurements.

In addition they were questioned about any change in their sense of well-being while on the drug. No placebos were employed and the double-blind method was not used. The patients selected were simply given the tablets and told they were to help them gain weight. They all were followed for a period of three months.

<sup>\*</sup>Produced by Syntex Laboratories under the tradename Anadrol.

Age and Sex of Patients. There were fourteen females and eleven males in the group. Of these four were between 3-15, two between 15-20, eight between 20-35, six between 35-55 and five patients between 55-90.

Diagnostic Categories. The patients selected fell into four more or less well defined diagnostic groups. These were:

- Gastrointestinal disorders (ulcers and colitis)
   —five patients.
- 2. Generalized arteriosclerosis—two patients.
- 3. Liver disorders (post-hepatitis and cirrhosis) —four patients.
- 4. Those with no clear organic disease but which were "chronically underweight" fourteen patients.

#### Results

Only two of the patients failed to gain any weight at all during the three month period of observation. Twenty of the patients stated that they "felt better" while on the drug although it is impossible in our opinion to rule out the role of suggestion here.

#### Results according to sex

Females gained an average of 2.9 lb./month.

Males gained an average of 2.2 lb./month.

#### Results according to age

Ages	3-15	gained	1.0	lb./month
	15-20	gained	3.5	lb./month
	20-35	gained	2.6	lb./month
	35-55	gained	3.2	lb./month
	55-90	gained	3.1	lb./month

#### Results according to diagnostic category

1. Gastrointestinal Group — gained an average of 3.1 lb./month.

- 2. Arteriosclerotic Group gained an average of 3.0 lb./month.
- 3. Liver Group gained an average of 3.3 lb./month.
- 4. "Chronic Underweight" Group gained an average of 2.4 lb./month.

Arm, Thigh and Girth Measurements. The twenty-three patients who showed weight gain all demonstrated an increase in these measurements varying from one to one and one-half inches depending on their age and height.

**Side-effects.** There were no side-effects noted in any of the group.

#### Typical Case

Mrs. R. N., age 73, had been treated for a gastric ulcer of the lesser curvature which responded to diet, antacid and antispasmodic medication and had healed. However the patient was markedly underweight (85 lb., height 5'1") and her family was interested in her gaining weight. She was placed on oxymetholone 2.5 mgr./three times a day and not only gained 2.8 lb./month but also stated that she had felt better while on this drug.

#### Conclusions

- 1. Oxymetholone in dosages of 2.5 mgr. one to three times a day produced an average of 2.9 lb./month weight gain in fourteen females and 2.2 lb./month weight gain in eleven males who had failed to gain weight on all previous measures.
- 2. Patients with organic pathology gained more weight than those who were "chronically underweight."
- 3. No side-effects were observed in the entire group of twenty-five patients.

800 Montana Avenue

# Perennial Allergic Rhinitis

STUART A. MASON, M.D., Odessa, Texas

One of the most common conditions the allergist sees in his practice is perennial allergic rhinitis. This disorder also is known as vasomotor rhinitis, hyperplastic rhinitis, perennial hayfever, and "all year round cold". The terminology often is used interchangeably to denote an allergic state involving the nasal membrane, characterized by sneezing, nasal itching, obstruction of the nose and watery nasal discharge. The nasal membrane has a characteristic pale, edematous appearance. The eyes may itch, burn, water, and appear reddened. Itching of the ears, mouth and nose may be present.

Patients commonly refer to this disorder as "sinusitis", but it should be noted that primarily the problem is that of the underlying allergy. Many complain of weakness, easy fatigue, lack of energy, and nervousness which they attribute to their "sinus". Cases of longer duration exhibit polyps in the nose and occasionally in the sinuses. Still later, the mucosa presents a granular appearance, and the nasal secretion, which formerly showed a predominance of eosinophils, now shows a change to polymorphonuclear leukocytes. An increase of fibrous tissue in the submucosa of the nasal membrane also occurs.

A characteristic allergic facies has been described in chronic nasal allergy. The face is flattened, because of flattening of the malar prominences. Children with allergies commonly exhibit the so-called "allergic salute"—caused by nasal itching and obstruction—by rubbing the hand against the nose. They also may sniff and wrinkle the nose.

The symptoms may be persistent or intermittent, depending upon exposure to the causative allergen. Emotional factors are present in some cases, while in others a change of temperature, especially going from warm to cold, may produce symptoms. The condition also has been known to occur during pregnancy, although the reason for its incidence at this specific time is unknown.

In arriving at a diagnosis of allergic rhinitis the history is most important, since the patient will often provide important clues to the etiology. Symptoms may be aggravated by contact with a specific type of animal, a cosmetic, a food, or when the patient enters a specific room in the house. He may be troubled more at work than at home, or while participating in a specific form of recreation, such as golf. He may state that other members of his family have the same condition, which is often referred to as "nasal catarrh".

Frequently he will be afflicted with other manifestations of allergy, such as eczema or urticaria. Examination of the nasal smear for eosinophils is a simple but helpful procedure. The patient is asked to blow his nose into a piece of waxed paper. The secretions are smeared on a glass slide, which is then stained with Wright's or Giemsa stain, and usually shows 10 per cent or more eosinophils.

In order to determine the specific allergens responsible for the symptoms, tests are done—either scratch or intradermal. It is generally felt that the scratch test is safer but less sensitive than the intradermal method. One also should bear in mind that the results obtained by testing must be correlated with the patient's history, and that both false positive and negative reactions occur. This is particularly true when testing with foods.

A patient who exhibits a positive reaction to a given food, such as chocolate, but who can eat that food with impunity need not be told to avoid that food. He may be told that he has a potential sensitivity to that food, and that he may or may not develop an actual sensitivity to it at some future date.

Beware of iatrogenic illness! Every allergist has seen, at one time or another, patients suffering from malnutrition incurred as the result of a faithful adherence to a diet based on the results of skin tests alone. Not infrequently the patient

will state that in spite of strict observance of the diet, the allergic symptoms have persisted. It should be pointed out that the results of skin testing, in the case of foods, leaves something to be desired, and that some allergists place greater reliance on the history obtained in a case of suspected food allergy than they do on the results of testing.

Most allergists feel that intradermal testing. particularly for foods, is more accurate than the scratch technique, and others feel that only certain methods of preparing the food antigens give accurate results.

The differential diagnosis of this condition includes hayfever, non-allergic forms of vasomotor rhinitis and infectious types of rhinitis.

Treatment consists of hyposensitization of the patient by injections of the antigens to which he is allergic. While his dosage is low he may be kept comfortable by administration of antihistamines, but as the size of the dose of antigen increases, it will soon be found possible to discontinue supplementary medication. Tuft<sup>1</sup> has stated, "The corticoids are of little and at best only of temporary value" in treating perennial allergic rhinitis.

One should not make the mistake of attempting to treat this condition by the administration of antihistamines alone, as the effect of the medication tends to wear off sooner or later, and the antihistamines are at best purely symptomatic treatment. They do nothing to prevent the development of complications of allergic rhinitis, and not infrequently are attended by side effects, such as drowsiness, which may under certain circumstances be dangerous. They are, however, a useful adjuvant to the specific treatment of the condition.2

Certain general measures must be taken to insure maximum benefits for the patient. If he smokes, he should be asked to stop, and to avoid smoky rooms, as well as other pungent odors, such as fresh paint, camphor, turpentine, and strong chemical fumes. If he is sensitive to dust he must observe definite dust precautions, in addition to taking his antigen by injection. He should try to avoid bringing into his room garments worn outside the home, such as shoes and overcoat. Special plastic coverings for mattress and pillow may be helpful. All foods containing substances to which the patient is allergic should be avoided.

It should be remembered that occasionally small amounts of penicillin are found in milk, a fact of considerable importance to the patient allergic to penicillin.

Indulgence in alcohol may produce an aggravation of symptoms. Over-exertion should be avoided, as well as unnecessary exposure to inclement weather. The patient should avoid persons suffering from respiratory infections, and under no circumstances should he take medication which has not been prescribed for him. It should be pointed out to the patient that his cooperation is essential if a good result is to be secured.

Sudden changes in temperature should be avoided. Abnormalities within the nose, such as deviated septum or nasal polyps, should be corrected. Infections, when present, receive appropriate treatment. In rhinitis associated with infection, the use of stock or autogenous vaccine may be very beneficial.3 Emotional factors must be sought after and treated as indicated.

If the patient understands the nature of his problem and if he is willing and capable of cooperating with the physician, a good result may be anticipated in the majority of cases.

#### Final Summary

Perennial allergic rhinitis is a condition met frequently in medical practice. Although it has a complex etiology, an adequate allergic history, followed by physical examination and skin tests. will usually provide the answer as to the cause. The cooperation of the patient during treatment is essential. Avoidance of causative factors, dusty and smoky environment, sudden changes in temperature and over-fatigue, are important, Nasal pathology, such as the presence of obstructing polyps and infection, must be corrected. When sensitivity to inhalants such as pollens and dust is present, appropriate hyposensitization should be undertaken. While this is being done, antihistamines may afford symptomatic relief, but they should not be used to the exclusion of specific hypo-sensitization.

1147 E. 42nd St.

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# Management of Endometriosis

W. E. LOCKHART, M.D., Alpine, Texas

An accurate diagnosis is important and not always easy to make, but the presence of endometriosis usually can be established clinically or at laparotomy, when it is often inadvertently found.

Management varies with the age of the patient, but not to the extent that we have been led in the past to believe. The notion has somehow gotten around that after a woman has reached forty it is all right to lop out uterus and ovaries, with little indication of necessity, and all will be well.

However, American women today who had good nutrition in childhood and were spared early debilitating disease by modern medicine often do not reach the menopause until near fifty. Preservation of the child-bearing potential is of greatest importance, of course, but—it should be added with emphasis—the sex life of the woman after the child-bearing function is past is also important.

#### Withholding Estrogen

The idea prevails that a woman of forty with endometriosis is best treated by ablation of uterus and ovaries followed by a period of strict withholding of estrogen, the theory being that the endometrial tissue which cannot be completely ablated will atrophy in the absence of estrogen. This may be true, but the atrophy is not limited to the endometrial tissue; it also attacks the sex organs and the entire physiological and psychological woman.

In addition, ablation of the ovaries and deprivation of estrogen leaves the woman highly susceptible to coronary atherosclerotic disease and to osteoporosis and degenerative arthritis. Here is a good example of treating the disease and ignoring the whole patient. Instead of there being a necessity to withhold estrogen, it is probable that the surgical management of endometriosis should be followed by high-dosage estrogen (100 mgm. of Stilbestrol daily) for several months, with a tapering off to a maintenance level.

In the literature one finds frequent reference to the endocrine treatment of endometriosis with brief, unsubstantiated remarks, such as: "The endocrine treatment of endometriosis is not considered very effective" or "is only palliative."

I have yet to find an article written by a doctor who says, specifically, that he administered 100 mgm. of Stilbestrol daily for six months without significant benefit to ten women with endometriosis. The treatment is not complicated and should be continued for at least three and preferably six months and can be repeated.

#### Value of Treatment

Many of the articles that play down the value of endocrin; treatment are written by surgeons, who, it seems to me, may be taking a dim view of a method which reduces the indications for a favorite operation. I once attended a meeting at which a Dr. Novak of Baltimore "regretted that Dr. Willard R. Cooke had become so unscientific" as to admit that the Stilbestrol treatment of endometriosis was effective in his cases.

Then, if the article originates in the vicinity of Houston, Texas, finding a surgical gynecologist who will admit that the endocrine method of treatment advocated by Dr. K. J. Karnaky has merit would tax Diogenes.

Another phantom to be exorcised is the carcinogenic reputation of Stilbestrol recently revived in Federal control of food contamination. There is no proof that Stilbestrol causes or aggravates cancer.

As for treatment with androgenic hormones or radiation, neither has any place in the treatment of endometriosis. A woman with normal adrenals will have plenty of androgen; it is doubtful if her normal amount should ever be supplemented.

401 N. Fourth St.

# Clinical Pathological Conference

R. E. Thomason General Hospital, El Paso

F. P. Bornstein, M.D., Editor Case No. 1672, November 16, 1961

Presentation of Case: Dr. NATHAN KLEBAN

History: Dr. L. GLADSTONE

Dr. Nathan Kleban: Doctor Averill A. Liebow, John Ely Professor of Pathology at Yale University School of Medicine, began his discussion of the case record of the Massachusetts General Hospital in this fashion: "It is fitting that on occasion the pathologist should be subjected to the same sort of intellectual karate (defined as: In Japan, a bare-handed contest) that our clinical colleagues sometimes suffer. This type of self-education is good for all." Doctor Liebow correctly diagnosed dissecting aneurysm of the pulmonary artery with rupture into the pericardium.

In this Latin border country we might change Dr. Liebow's hyperbole to intellectual "corrida de toros", recognizing the "el toro" might be an awkward runt detouring briefly from the slaughter house chute and el torero un novillero lacking courage, grace and accuracy.

I am grateful to Dr. Bornstein for this monthly corrida, which, to me, is a stimulating and enlightening teaching form. Our recorded clinical record is all too frequently bare and blurred. In a broad sense, it is a reflection on the standards of our entire medical community. My critical comments are made from the omniscient summit of retrospect.

#### History:

Dr. L. Gladstone: A 56-year old widow, who had had no vaginal bleeding for 27 years, and who had five surviving children of the eight to which she gave birth, died on Sept. 22, 1961, two months after she was first seen here. The duration of her illness we do not know.

Probably unrelated directly to her fatal disease was an admission to this hospital in 1956 when she complained of vertigo, had pyuria, and was given a discharge diagnosis of cystitis. Any addi-

tional information from her microfilmed chart would have to be obtained by one with less feeble vision than my own. If the secret to her disease, or for that matter, the password to Nirvana or Paradise, were written on that record it is safe from my shifty, cloudy, presbyopic eyes.

On July 17, 1961 the patient was referred here by a physician for workup with provisional diagnosis of anemia and congestive heart failure. The patient mentioned right abdominal pain, poor appetite, and constipation. Although no evidence of congestive heart failure was found on physicial examination, there seemed to be x-ray evidence of this condition. The only reference made to shortness of breath was in a progress note, which stated that the shortness of breath had improved.

At this time, Dr. Stokdyke, I would like for you, if you will, to interpret for us the x-ray made on her first admission in July.

Dr. Glen A. Stokdyke: As you can see from the film, this is not a routine film. It is a supine film and so the true degree of cardiomegaly is not directly measurable with the variables that we have, but apparently this does represent severe cardiomegaly of generalized type, generalized cardiac enlargement, and, as we see, incipient pulmonary edema.

We have to realize, of course, that on a supine film we are not going to be able to see obscuring of the angles that we would expect to see if there were actual pleural effusion leering out along the angles, and so there may actually be more effusion at this time which is not at all apparent. So I termed it incipient pulmonary edema.

If you look in retrospect here we see a nodule about one and one-half centimeters. However, even looking rather carefully, it is a little difficult to distinguish it from the hypervascular marks in general at this time.

**Dr. Kleban:** She had a flat film of the abdomen: why don't you review that one also?

Dr. Stokdyke: Here the supine film of the abdomen reveals degenerative change. You see the sclerosis above the symphysis pubis, which may or may not represent osteitis pubis. I am certainly no expert in this region. However, I think the symmetrical character and the light does tend to rule out quite well its being an osteoblastic metastasis.

As we see in the record, the renal and psoas shadows are fairly well visualized, considering the amount of fecal matter in this rather obese female. I believe the renal shadows are fairly well seen. The right may lie a little lateral, and then I mentioned a sigmoid configuration of calcification in the right upper quadrant. It was not apparent at the time just what the significance of this was on this single film.

**Dr. Kleban:** The record does not state why a supine chest film was done, and apparently she went to the radiology department for it. It does not state that she was not able to sit up, or that she was not able to stand, so we really don't know why that was made supine.

The patient was found to have an abdomen which was large, difficult to examine, distended, and tender in the lower quadrants. There was a mild edema. There was pyuria. The electrocardiogram was normal. The patient was given belladonna, phenobarbital, Diuril. Aerosol was prescribed. Her buttock was needled by the white magic of penicillin. Digitoxin was prescribed in a maintenance dosage. We do not know that she had been digitalized before entering the hospital. She was not digitalized here.

The day before discharge the patient refused a meal, warned it would make her vomit, but she puked anyway. She was vomiting on the day of discharge. She also complained of back pain before she left the hospital. It must have been pretty hot one night that she was here, because the patient removed her gown and fought the attendant who attempted to keep her covered with a sheet. I don't know how this is related to the course of her illness.

She was given Achromycin for the road when

she departed, possibly as a charm against unfriendly microbes which she might have carried away with her from Thomason General Hospital.

Eighteen days later she returned to medicine clinic complaining of weakness. Hydrodiuril with potassium and digitoxin were continued.

Twenty-two days later the patient reentered the hospital, still too weak to walk, with right flank pain that moved to the left side, with vomiting, but with no fever and no diarrhea. At this time there was upper abdominal tenderness. One examiner described tenderness in the right upper quadrant. Hematocrit dropped from 37 to 31. Hemoglobin from 11 to 8.5. There was no fever. Penicillin was again injected. One unit of blood was transfused.

Suppose we look at the x-rays which were made on this admission, Dr. Stokdyke, if you will. Again she had the chest x-ray and an effort was made to obtain gallbladder x-rays.

Dr. Stokdyke: At this time we see that the treatment apparently has resulted in clearing of this incipient pulmonary edema, which I mentioned, but it appears that there are numerous roughly round variegated dense cysts occupying primarily the lower half of both lung fields. The heart is still slightly enlarged but we don't see any evidence of pleural effusion. The angles are quite clear. The thorax appears to be within normal limits.

As you see in the protocol, I did mention that this appeared to be metastasis to the lungs at this time. Apparently the x-ray reports take up the bulk of the protocol here, and I don't know if I can say it in any less time than it may be copied or read by you. I seem to be agreeing with myself pretty well upon looking at the films here, and we see the telepaque scattered about the film of the abdomen here, with no evidence of dye concentration in the gallbladder. However, the patient has been cleaned out considerably. For all I know she may have lost some weight, and it becomes fairly evident that these represent two roughly round laminated gallstones at this time.

Of course, the fact that the gallbladder is nonfunctional probably helped me to decide this (although not so much as if they had any functioning gallbladder.) This would, of course, have been a real clincher. The osteitis pubis has not changed appreciably. Here we see evidence of a soft tissue mass which lies in the right upper quadrant, and upon looking at the previous film was probably also obvious at this time. I think one of the greatest omissions people in x-ray and people who look at the x-rays can commit, one of the greatest crimes of omission, is that of comparing with previous films.

So if you may look at it you can see that this was probably present on the previous film, but, again, the dirty bowels pretty well covered the lower and medial border a good bit. Here we see the medial border extending up to the level of the second lumbar vertebra, and no doubt to the left of it even. I believe it can be distinguished from the liver shadow quite well. This is probably the lower edge of the liver right here, as opposed to the soft tissue mass lying here, and better seen on the lighter film here.

Dr. Kleban: We will hold that for our last admission. The patient had a drop in blood pressure and received Coramine during this admission.

Goodman and Gilman state that Coramine, which is nikethamide, is used in shock-like conditions, but that it has an undeserved reputation as a cardiovascular stimulant. They don't think it is of much value clinically, although it does increase cardiac output in a dog with less mechanical efficiency.

The patient had headache and nausea, refused her diet at this time. Although it was still August, she kept the covers over her head. She vomited. She had a large soft dark brown stool and urinated in bed. She was discharged with a diagnosis of gallbladder cancer, metastatic to the lung.

Apropos of making a diagnosis of malignant disease on the basis of evidence which does not include histological material, there was recorded in 1950 a series of cases from New York. It was there at Mt. Sinai or one of the New York Hospitals, in which these individuals reviewed 20 patients referred to them, in whom one of these three conditions existed: 1. A diagnosis of terminal cancer was made with no cancer present; 2. A diagnosis of terminal cancer was made although curable cancer was present; and 3. A diagnosis of cancer was not made although a visible lesion was present for a long time.

The author suggests the point of view of taking

nothing for granted.

Our patient returned to this hospital fifteen days later with labored breathing. Her white blood cell count was slightly elevated. Her hematocrit and hemoglobin were unchanged. Proteus was grown from the urine but there was no urinalysis. She had no fever. She was cyanotic, stuporous. Demerol was prescribed for pain, although we are not told on the chart where her pain was. She had bloody vomitus before she died.

Doctor Stokdyke, will you tell us about her final x-ray film. I believe there was just the chest film on this admission.

Dr. Stokdyke: That's all. I am speaking slower than I usually do for the benefit of our young lady up here. I hope I am not dragging it out too much.

I made a point of saying that there was no pleural effusion on the two previous films, and here we cannot visualize hemidiaphragm, which is pretty good dictum when you can't visualize either diaphragm. You either have dense pleural adhesions obscurring the bases or you have free fluid, and here I started out by saying the reexamination again with a portable film of the chest reveals marked pleural effusion occupying perhaps the lower two-thirds of each lung field, and considerable infiltrate in addition in the upper third.

You will recall that the metastatic lesions were not particularly evident in the upper third, so I went on to state, to remind ourselves, that the previous films did reveal bilateral nodules already likely metastatic, infiltrate of both lower lung fields. Then I hazarded the guess that the pleural effusion was likely on this basis, although the patient, we know, has had cardiomegaly previously. It is quite uncommon to have this much pleural effusion just on the basis of cardiac failure alone.

Dr. Kleban: Thank you Doctor Stokdyke.

We met this lady on microfilm for the first time five years before admission, at which time she apparently had cystitis. Lower urinary tract complaints did not recur. Despite the presence of pyuria, 20-30 W.B.C on her first admission in 1961, and 10 to 12 W.B.C. on her second admission, and Proteus grown from the urine, on third admission; the absence of fever, the absence of an

elevated blood pressure, and the absence of a significant leukocytosis, plus the difficulty of explaining the lung disease, eliminate to me pyelone-phritis as the primary fatal disease although it was probably an incidental autopsy finding.

We cannot ignore entirely the possibility of carcinoma of the gallbladder. Stones are present in the region of the gallbladder. In the Surgical Clinics of North America for October, 1959, McDonald, Southwick and Cole, in an article entitled, "Prophylaxis Against Cancer in the Gastro-Intestinal Tract," say "the elective removal of calculous gallbladders as a prophylactic measure to prevent carcinoma of the gallbladder is a controversial subject". Stones have been found in 64.6 per cent of 212 cases of carcinoma of the gallbladder.

Carcinoma of the gallbladder has been found in surgery for gallbladder disease in an incident of .5 to 2.3 per cent. In autopsies from Massachusetts General Hospital the incidence of carcinoma of the gallbladder in gallbladder disease runs about four per cent. These particular authors, who are surgeons, believe surgery for asymptomatic gallbladder stones should be done if expected long-evity is seven to eight years or more. The disagreement about this is not among surgeons. The disagreement is between surgeons and non-surgeons.

Although the incidence of cancer of the gall-bladder is low, there has usually been local spread to the porta hepatis area when the patient comes to surgery. Invasion of the common bile duct with laboratory or clinical obstructive jaundice is almost invariably present when the patient is operated on. Metastasis is local to the liver and surrounding region rather than to the lung.

I believe the lady's gallbladder failed to visualize because the contrast medium was not absorbed from the gut. Double dose, special techniques or I. V. contrast medium injection must be done, and one must know that the liver is capable of picking up and excreting the material before one can conclude that the gallbladder is unable to concentrate the radio-opaque material. I do not believe this lady had cancer of the gallbladder.

That this disease is not primarily infectious in the lung is supported by the absence of signs of infection, cough, sputum. We have no knowledge of thrombotic disease of the veins in this lady. The patient was not confined to bed prior to onset of the present illness that we know about, although there is nothing against multiple areas of pulmonary infarction on the chest x-ray made during her August admission.

The cumulative evidence is overwhelming for the interpretation which I have chosen to explain the course of events.

The early phase of this woman's illness was obscure. Her appetite was poor, but she did not waste away as one would expect with malignant lesions of the stomach or of the liver. The pain was vague, and somewhere in the right flank, the right upper quadrant or right lumbar region. She apparently had some complaint of trouble with her breathing, although the early reference in the chart is oblique and has to be searched for in the record.

She had no physical signs of congestive heart failure early, and for some perplexing reason this film was made supine, presumably at a distance of about 40 inches. This leads to misinterpretation of cardiomegaly and early pulmonary edema. The electrocardiogram was normal, Respiratory symptoms were probably due to malignant embolization to pulmonary blood vessels.

Although not palpable until her final admission, there was a mass in her upper quadrant, interpreted as gallbladder, but which I prefer to interpret as right kidney. One can make out this lateral border of the mass fairly well. Now, Doctor Stokdyke follows the particular mass over the spine. I prefer to interpret that mass as a kidney rather than as a gallbladder. Hematuria was present as a terminal event and does not contribute to the classical triad of hematuria, flank pain and a flank mass.

An analysis of 100 histologically proven cases of renal cancer from records of the New York Hospital, Cornell Medical Center, gives this information: The peak incidence of cancer of the kidney in this series was in the age group of 50 to 60 years. Cancer was present in males over females in a ratio of two to one. Gross hematuria was present in 58 of the 100 patients.

Twelve of these 58 patients did not notice the hematuria themselves. In one individual the hematuria was microscopic only. Calcification was noted in 7 per cent. A mass was noted in only 15 of the 100 patients. Thirty-three of them. or one third, had no clinical indication of renal disease of any kind.

The classic triad of flank pain, hematuria, and flank mass was present in only 10 to 15 per cent of the 100 cases. Pain was present in less than 20 per cent. Cancer of the kidney was discovered at autopsy while not suspected during the life in five individuals.

The type of illness which these one hundred patients seemed to have was one of intermittent episodes of non-specific symptomatology. Of them, two had polycythemia which disappeared after nephrectomy. Papanicolaou's smears were not helpful in making a diagnosis. In one there was a horseshoe kidney. In one there was a general sarcoidosis.

Two had leukemia in addition to cancer of the kidney. Fifty-eight had enlarged kidney or a mass. Fifty cases were presented to five radiologists who didn't know the diagnosis. There was a 50 per cent correct diagnosis. The five radiologists agreed in only 10 per cent of the fifty cases. These particular authors claimed an accuracy of 94 per cent with nephrotomography.

Melicow and Uson report on 577 malignant renal neoplasms; about one-third had non-uro-logical symptoms. The most common symptom was weight loss; the next most common was pain, and the pain was usually at the site of metastasis. Lucke and Schlumberger state that malignant tumor of the kidney constitutes about one to two per cent of cancer of all sites. The types of renal neoplasm are carcinoma in 83 per cent, renal pelvic malignancy in eight per cent, and nephroblastoma or Wilms tumor in six per cent, with sarcoma in three per cent.

C. D. Creevy wrote in 1935: "Malignant renal tumors should be classed with syphillis and tuberculosis as among the great minics encountered in clinical medicine. By direct pressure or by necrosis or hemorrhage, by extension or by metastasis they can reproduce the clinical appearances of an amazing variety of disorders".

Early spread of renal cancer to the lungs is common. The patient may have had congestive heart failure. I do not think that the electrocardiographic changes were sufficient to support a diagnosis of primary coronary artery disease.

She may have had a Mallory-Weiss syndrome.

She had been vomiting for a considerable period of time and may have had lacerations of the lower portion of her esophagus or the cardiac portion of her stomach.

My diagnoses then are: Carcinoma of the right kidney with pulmonary metastases, bronchopneumonia, pyelonephritis, coronary atherosclerosis, and gastric erosion.

**Dr. Bornstein:** Thank you, Doctor Kleban. It is customary at this time to ask for additional comments. I just wonder what is left to say. Carcinoma of the kidney being the main diagnosis of Doctor Kleban, does anyone care to make any comments?

Dr. H. M. Gibson: Could we have those films put back up there again?

Dr. I. S. Heinemann: I will stick my neck out with Doctor Kleban here. It is probably "hypernephroma" or adenocarcinoma of the kidney. I would like to add to what he said that pyuria is not an infrequent finding with a renal tumor. I would also like to stick my neck out on this fact: Whenever you have a KUB film, even though you see the outline of the kidney, a tumor that sticks out in front or posterior frequently will not be seen. You can't rule it out just on a KUB on the smooth, lateral or medial surface. The other thing is you can't differentiate intraperitoneal and extraperitoneal tumors on just a KUB film. I think it takes at least a pyelogram with oblique, lateral films to do this.

Dr. Gibson: Certainly you can see the shadow of the left kidney. The right kidney shadow does appear to be taken up by this very, very large mass. The two opaque shadows, sitting one on top of the other, are circular. They could very well be gallstones. However, there is a remarkable consistency between the two films, as far as the precise position of these shadows. I believe that this patient most likely had a carcinoma of the kidney, and I would like to say that these shadows look very suspicious of some sort of arterial lesion such as an aneurysm of the renal artery.

Dr. Bornstein: Is there any further discussion?

Dr. Jack C. Postlewaite: What about the evidence that she is Spanish-American, she is 56 and she is obese. I just want to make sure they didn't omit carcinoma of the gallbladder.

Pathological Discussion: Dr. Bornstein Autopsy revealed an elderly woman with a large and distended abdomen. After the usual incision, I noticed fibrin and serous fluid in each pleural cavity and a small amount of fluid in the peritoneal cavity. The margin of the liver was located about two cm below the costal arch. The first thing that came to my attention was a rather large heart which weighed 550 grams. It represented a typical hypertensive heart.

The next unusual finding was in the liver which weighed 2400 grams. The liver was deep brown in color, and on section had the same deep brown color. The markings of the liver were obscured. Both lungs were enlarged and covered with very large tumor nodules which measured up to five cm in greatest diameter. The only other remarkable finding in the lung was atelectasis of the lower lobe.

The interest naturally was attracted to the mass in the right lower quadrant. The mass was a very large one. It measured 20 x 15 x 12 cm and weighed 1200 grams. On sectioning one could see that the mass compressed the right adrenal gland. The cut surface showed a tumor mass measuring 15 cm in greatest diameter. On surface of the tumor there was a small crescent of about three to four cm in width, representing a light brown kidney parenchyma.

The kidney parenchyma was fairly firmly attached to the tumor and the tumor obviously arose from the kidney. The tumor on cut surface had a rather variable appearance of grey, reddish and bright yellow necrotic areas which produced peculiarly intermixed patterns. Those were the most important findings on gross autopsy.

On microscopic examination of the tumor a rather peculiar histological pattern was found. The pattern in some areas was a typical carcinoma of the kidney. On other slides, however, the pattern was composed of elongated spindle-shaped cells which nearly could have been taken for a primary sarcoma.

Perhaps of all epithelial tumors, kidney carcinoma is the one which mimics sarcoma easiest. I remember that recently we had an amputation of the humerus, and simply from examining the humerus one would have gotten the impression of a primary osteogenic sarcoma. However, there

was unquestionable evidence that it was a metastasis of the clear-cell carcinoma of the kidney. So much about the tumor.

In addition there was a strikingly brown discoloration of the liver, splcen, and adrenal glands. Section from those organs, especially of the liver and adrenal glands, revealed the presence of a diffuse amyloidosis. I personally consider this amyloidosis a secondary phenomenon and of no particular consequence in this case.

As was discussed, the patient had signs of cardiac failure which are explained by the hypertrophied hypertensive heart and the pleural effusion indicative of the fact that the patient was in cardiac failure.

Clinical Diagnosis: Carcinoma of gallbladder with metastasis to lung.

Dr. Kleban's Diagnosis: Carcinoma of the right kidney with pulmonary metastases. Bronchopneumonia. Pyelonephritis. Coronary atherosclerosis. Gastric erosion.

# Final Anatomical Diagnoses:

- 1. Carcinoma of right kidney with direct invasion of adjacent soft tissue and metastases to both lungs.
- 2. Cardiac hypertrophy, hypertensive type, associated with pleural effusion, bilateral.
- 3. Amyloidosis of liver, spleen, adrenal glands and kidnevs.
- 4. Chronic cholecystitis and cholelithiasis.

Dr. Bornstein: If there is no additional discussion, I think we should close the meeting by giving applause to Dr. Kleban who gave us such an outstanding presentation of this case.

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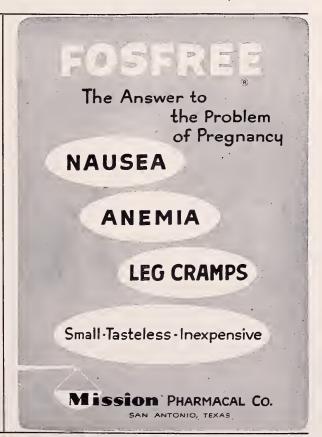
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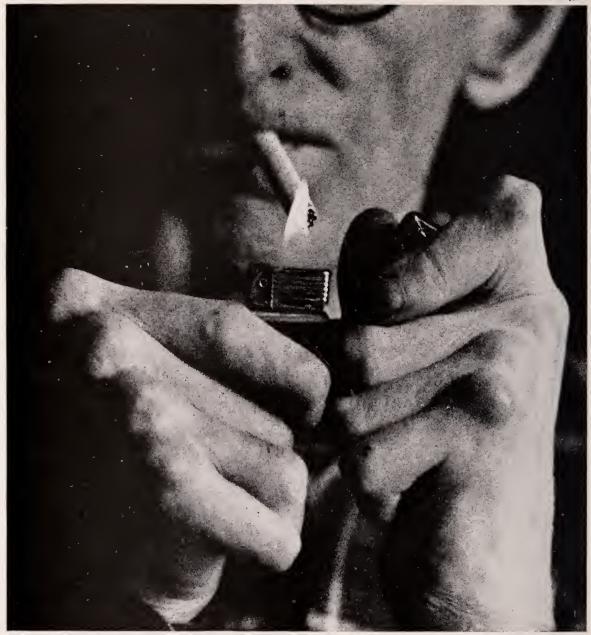
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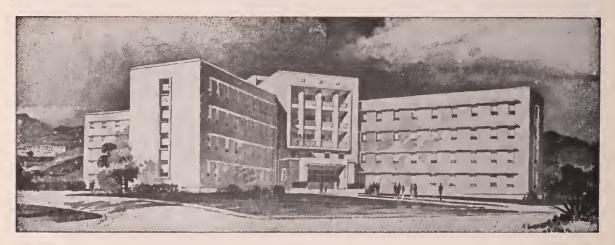
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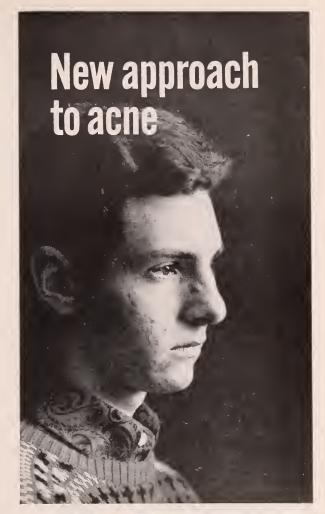
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The Western Association of Railway Surgeons, annual meeting, Stockmen's Motor Hotel, Elko, Nev., Sept. 27-29, 1962.

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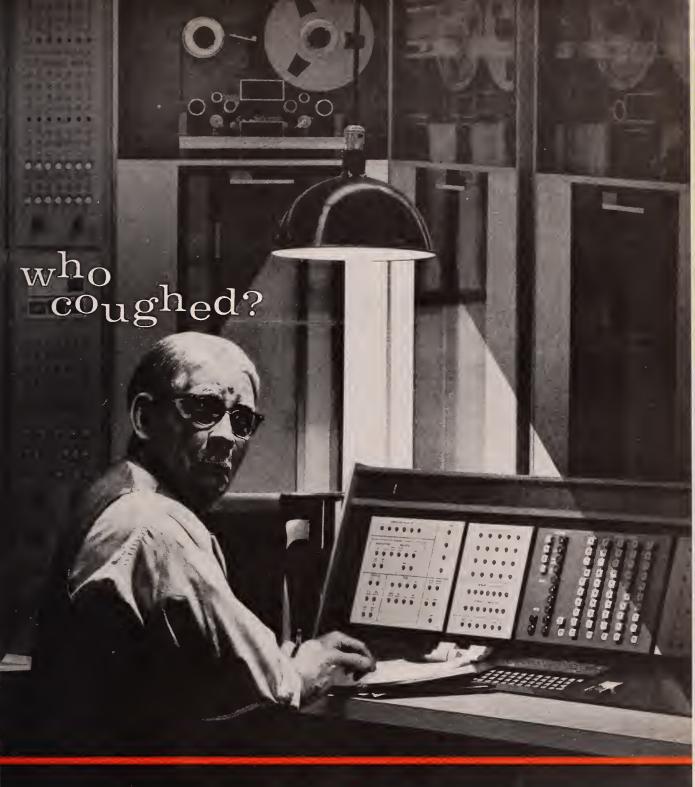
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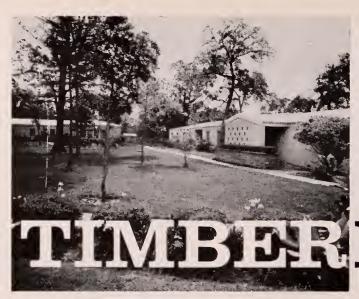
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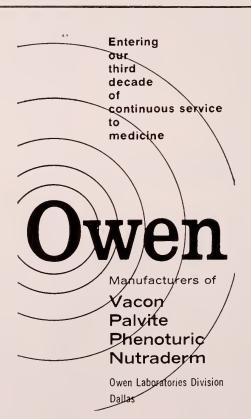
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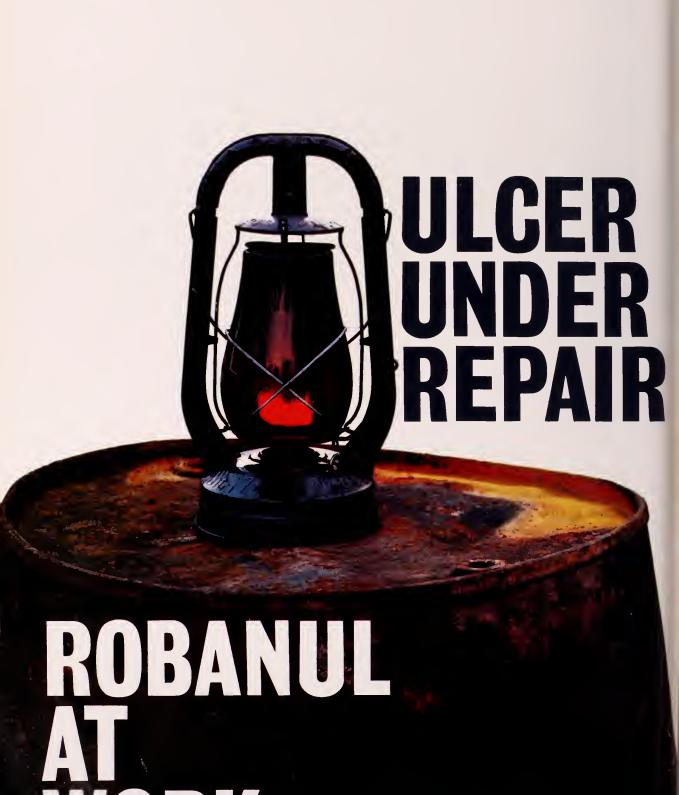
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# Diagnosis of Carcinoma in Situ of the Cervix\*

CARY M. DOUGHERTY, M.D., and NADALYN COTTEN, B.A., New Orleans

Department of Obstetrics and Gynecology Louisiana State University School of Medicine

The increased use of detection measures for the earliest stages of carcinoma of the cervix has resulted in the finding of many more of these lesions. In addition, more instances of borderline states and precursors of cancer are being encountered. With these findings and with observations on the course of treated and untreated disease our concept of the nature of cancer disease of the cervix is undergoing reorganization.

No longer can we say that every patient either has or doesn't have cancer. Some are being found to have lesions which can best be described by such unscientific terms as mild cancer, even questionable cancer.

How can this be? How has this change in thought from the old jet-black — snow-white concept to the newer grey-zone identification come about? Not long ago the generally accepted definition of carcinoma of the cervix was an uncontrolled proliferation of the epithelium which, left untreated, continued to spread in all directions and in all tissues until it destroyed the person so afflicted.

Almost fifty years ago, European and American investigators began to recognize conditions in which neoplastic proliferation of epithelium was confined to the surface only. It was soon learned that, excluding the property of invasion, masses of cells in the one growth were not distinguishable from masses of cells in the other one. This thought of

morphologic identity has been substantiated by the finding in cytologic smears from the cervical and vaginal secretions of identical types of malignant cells originating from the two lesions in question.

For a period of time surface malignancy, carcinoma in situ, was accorded the dignity of its own name and was considered to be a separate entity. Many authorities were unwilling to consider it as a part of cancer disease. Since the two conditions were considered separate, differences of opinion arose over the earliest point at which invasive growth occurred. Thus appeared the first of two fuzzy zones in diagnosis, that is, the point where the disease went from hasn't to has cancer.

# Second Zone

More recently, a second grey zone has developed in the diagnosis of early cancer. Its appearance came about in a manner similar to that traced for the first one. After general agreement of a sort was reached in the definition of surface and invasive cancers, observers began to note that in some instances cervical tissues contained diseased epithelium similar to but apparently not so markedly diseased as that in outright surface malignancy.

On cytologic smears one could see irregularity, density of staining quality, and alteration of the normal ratio of the sizes of nucleus and cytoplasm. in cells of the cervix. These changes are not always of the same degree in different smears and in some cases the degree of change is decidedly less than that required for the diagnosis of malignancy.

<sup>\*</sup>From the Walter E. Levy, Jr., Memorial Laboratory for Gynecological Pathology, Supported in part by a grant from the Greater New Orleans Cancer Association, Inc.

Smears containing these cells could not be called positive for malignant cells, nor could they be called benign smears. The appearance, then, of epithelium showing anaplastic alterations and the finding of smears with atypical cells brought about the identification of another early phase of cancer disease, i. e., dysplasia, or atypical hyperplasia.

The pathogenesis of early cancer of the cervix appears to be about as indicated in this diagram:

Normal epithelium — dysplasia — carcinoma in situ — invasive carcinoma.

Considering these abnormal states as increasingly severe phases of a single disease one is able to plan treatment of increasingly wide scope. More important, one must use this concept in order to understand and interpret the findings of cytologic and histologic material. To give an illustration of the way in which one phase gradually merges into the next without sharp transition one need only note the terms which have been suggested in medical writings in recent years.

One sees the descriptive labels of mild, moderate, or severe dysplasia; differentiated or undifferentiated form of carcinoma in situ; and carcinoma in situ with early stromal invasion, carcinoma with minimal invasion, or microcarcinoma. These attempts at grading the severity of disease indicate that the changes are gradual with no steps marked out.

# Series of Changes

Keeping in mind, then, that cancer disease probably is characterized by a series of changes within the epithelial cells and masses of these cells beginning with alterations of minimal degree and progressing smoothly to changes of the greatest degree, we can map areas which we will designate by the names listed above. In establishing criteria for the diagnosis of carcinoma in situ it is necessary to bound this phase of disease on each side, the dysplasia side and the invasive cancer side.

We put this hypothesis to work in the Department of Gynecology at Louisiana State University School of Medicine approximately ten years ago. In order that our observations could be made consistent over a period of years, type cases were selected and descriptions were recorded of the various epithelial lesions.

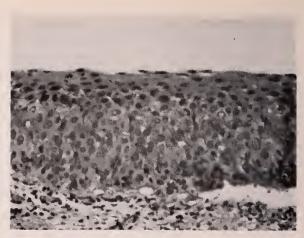


Figure 1
Epithelial atypism, severe degree.

Epithelial atypism was diagnosed when these features were seen (Fig. 1): Crowding of cells but with a noticeable differentiation from basal to superficial layers; loss of polarity of cells but with a definite tendency toward normal orientation of cells in the upper layers; more deeply stained nuclei but not of the most intense degree; mitotic activity increased over normal amount; disappearance of glycogen from the intermediate and superficial cells; and in some instances presence of unusual and irregularly shaped cells; and nuclei. Cytologic changes in smears from epithelial atypism are those of superficial and intermediate dyskaryosis.

Carcinoma in situ was diagnosed when the following features were judged to be present (Figs. 2, 3): Crowding of cells in all cell layers; loss of polarity, or vertical orientation of cells within the epithelium; deeply stained nuclei of the most in-



Figure 2 Carcinoma in situ.



Figure 3
Carcinoma in situ with hyperkeratosis.

tense degree; greatly increased mitotic activity; and, in some instances, presence of bizarre and irregularly shaped cells and nuclei.

The diagnosis of carcinoma in situ was not excluded in some cases where there was minimal evidence of differentiation of cells toward the surface or where there was abnormal keratinization (Fig. 3). Scrapings of the cervix with carcinoma in situ examined cytologically show positive malignant cells as well as dyskaryotic superficial and intermediate cells.

Eary invasive carcinoma, the next full degree of increasing severity after surface growth, is characterized by a relatively abundant proliferation of malignant cells with obvious penetration into the connective tissue space of the cervical stroma (Fig. 4).

At times it is difficult to decide whether a given



Figure 4
Early infiltrating carcinoma.

mass of cancer cells is within a cervical gland or whether it has invaded the connective tissue space. In cases of doubt it is safe to proceed with the more conservative treatment. On this point there is fairly general agreement among the experts in the field of gynecologic pathology. The finding, however, of unequivocal invasion is the signal for full treatment, either full radiation or radical hysterectomy.

While not changing the criteria for diagnosis of each of the above phases of the disease, the amount of abnormal epithelium actually seen did influence the judgment of the borderline cases. When a

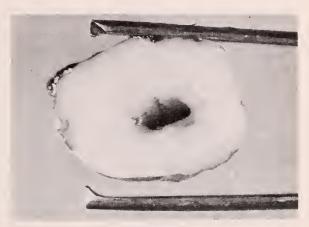


Figure 5
Cone of cervical tissue removed by scalpel.

large quantity of diseased epithelium was present in an adequate specimen of cervical tissue, the tendency was to advance the diagnosis. When a small amount was present the tendency was to assign a diagnosis conservatively.

# Definitive Diagnosis

Sharp conization of the cervix has been and remains our principal means of obtaining a definitive diagnosis of carcinoma in situ. We remove a cone of tissue (Fig. 5) by means of a sharp pointed knife, striving to remove the external os and lower half of the endocervix. Opening the cone at its thinnest portion we place it flat on a piece of chipboard or trim it with a razor blade into blocks (Fig. 6) which are individually flattened against cardboard tags and fixed in Zenker's or formalin.

My own preference is for the method of trimming in the fresh state and mounting on cardboard

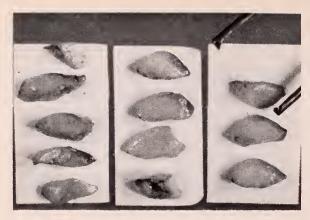


Figure 6

Twelve blocks of tissue from the cone of tissue in Fig. 5. Each block is mounted flat on cardboard tag so that a flat surface will be obtained for sectioning. The epithelial surface is the smooth, curved side of each block, and is perpendicular to the flat surface in each instance.

for fixation. In this way we obtain well-oriented blocks no matter how ragged the tissue received from the operating room. One to five sections are prepared initially from each block (Fig. 7). I would like to emphasize that the preparation of a good specimen is absolutely crucial in obtaining a pre-treatment diagnosis.

In my opinion, the weakest part in all the management of carcinoma in situ is the dependence upon mediocre histologic sections which are poor because of one or more faults in securing or processing the specimen of cervical tissue. This is certainly true in our own department.



Figure 7

Five paraffin sections cut from each of the twelve blocks shown in Fig. 6.

Using the criteria as outlined we have recorded our experience with carcinoma in situ since 1958. Table I shows the occurrence yearly.

Table I Occurrence

Number of Cases Diagnosed Each Year

	Ca in Situ	Ca I-IV*		Ca in Situ	Ca I-IV
1948	1	72	1955	18	79
1949	2	76	1956	33	75
1950	9	62	1957	. 36	80
1951	9	63	1958	. 37*	90
1952	6	65	1959	21	64
1953	17	70	1960	17	70
1954	22	83	1961	16	66
		TC	TAI	. 244	1015

Clinical carcinoma of the cervix occurred 1015 times in the same interval of time. Atypical epithelial hyperplasia has been recorded since 1952, during which time 436 instances of this disease have been found. Malignant disease of the cervix was pursued by means of Schiller stain and biopsy, cytology, colposcopy, and finally, microscopic examination of surgical specimens.

# **Observations**

Age and parity of the patients having carcinoma in situ are shown in Table II.

Table II

Age		Parity		
Average	38.6	Parous	.232	
Youngest	20	Nulliparous	12	
Oldest	82			

The disease is one of the latter part of the reproductive age, while the fact of having borne children predisposes a woman to its development by a factor of about seven times (assuming there are three parous for every nulliparous woman in the general population).

The means by which patients came under study leading to the diagnosis of carcinoma in situ are listed in Table III.

Table III

Discovery of Lesion

Cytology	93
Colposcopy	31
Biopsy	166
Unexpected finding	21

<sup>\*</sup>Tumor Registry, Charity Hospital of Louisiana in New Orleans.

The only weapon continuously used was biopsy. The other methods of detection were used at times when the facilities were available. In reference to the accuracy of the two main means of diagnosis Table IV gives the correlation of the first Pap smears in each case with the tissue diagnosis of carcinoma in situ.

# Table IV First Cytology

Tissue Diagnosis	I	II	III	IV	1,
	_	_			_
Carcinoma in situ	6	17	61	38	16

Cytology was done in 138 patients having this disease. There were four per cent clean misses, P I, and 84 per cent clean hits, P III, IV, V. Twelve per cent of the smears were alarming but not positive. Table V depicts a corresponding evaluation of first biopsy.

# Table V First Biopsy

Tissue Diagnosis	Cervicitis	Atypism	Ca in situ
Carcinoma in situ	14	47	150

Seven per cent did not show any evidence of the malignancy, 22 per cent were indecisive or showed only atypical hyperplasia, and 71 per cent were confirmatory. A fact to remember here is that biopsy is not the court of last resort in every instance. Two successive biopsies or two cytologic examinations would closely approach an accurate appraisal of the condition of the cervix, but a single trial of either method appears to miss a portion of the cases of this disease.

To obtain a complete diagnosis in each patient it is necessary to examine the uterus when the patient is treated definitively. Until that examination is carried out one is not sure of the total extent of the growth or whether there are multiple foci of origin of the growth in the cervix. Table VI shows the results of histologic study of the uterus after removal.

# Table VI Ca in Situ in Hysterectomy Specimens

Unexpected finding at hysterectomy for	
other condition	21
Diagnosis made at hysterectomy after	
negative biopsy and cone	8
Residual disease in uterus after positive	
biopsy or cone	71
No residual disease in uterus	100

The unexpected finding of carcinoma in situ is. we are happy to say, decreasing yearly with the increased use of detection measures. Residual disease was found in the uterus in three out of seven specimens while four of every seven were free. In a few cases the definitive diagnosis was not obtained until the specimen was removed. Most of these patients had contradictory biopsies or several indeterminate cytologic smears, or for some other reason they were managed in a fashion outside of the usual routine. One might consider that in these patients there is the example of prophylactic livsterectomy.

# Summary

- 1. In order to make fullest use of detection measures of early cervical cancer it is necessary to have a knowledge of the pathogenesis of the disease.
- 2. Graded degrees of severity of disease require graded methods of treatment. There are no sharp boundaries for and no large gaps between the conditions of dysplasia (atypical epithelial hyperplasia), carcinoma in situ, and early invasive cancer.
- 3. Although there are no firm objective boundaries of each of these phases of cancer disease, each one is characterized by features which make identification fairly uniform. Instances of disease which lie close to the bounds constitute a "grey zone," where differences of opinion exist as to the diagnosis.
- 4. Since there appears to be only a quantitative difference between lesions located in the grey zone the clinical management and the prognosis are not greatly different in cases falling close to the borderline on both sides.
- 5. Final tissue diagnosis is not complete until the uterus is examined histologically in instances of carcinonia in situ.

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# Reconstruction of the Paralyzed Upper Extremity

The Use of Certain Operations and Surgical Techniques

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Surgical procedures in the upper extremity subsequent to paralytic poliomyelitis can give most gratifying results in restoring some function, converting a useless extremity into a useful member. Certain operations at various levels will be considered.

#### Shoulder

Scapulohumeral arthrodesis is frequently indicated in deltoid paralysis. A hand must have proximal stability in order to be useful and fusion of the shoulder can sometimes help to restore this. Even if the entire extremity is very weak, the operation may be useful to keep the patient from catching his arm when turning over in bed. The trapezius and serratus should function in order to activate the fusion.

The 1942 report of the Research Committee of the American Orthopedic Association outlined the indication and pointed out that the best range of motion is obtained if the patient is operated before age 12. This survey also, surprisingly, revealed that although growth disturbance of the proximal humeral epiphysis was expected, this did not occur in their survey of 101 cases.<sup>1</sup>

I have found the following points of technique useful: The application of a cast preoperatively, with the upper extremity in a salute position, facilitates the surgical procedure. This cast, which is bivalved and removed immediately prior to surgery, can be reapplied and taped into position at the conclusion of the open surgery.

The incision should be an adequate one over the end of the shoulder. There is no danger of nerve injury since the deltoid muscle is nonfunctional. Excision of the end of the clavicle gives a greater range of motion.<sup>4</sup> Internal fixation with the use of staples as well as a Crowe point pin has been most useful in obtaining the desirable position of 45 degrees of glenohumeral abduction, 45 degrees of forward flexion, and 25 degrees of the forearm above the horizontal with the hand held in front of the face. It should be noted that this position of 25 degrees above the horizontal is actually a position of internal rotation in relationship to the anatomic position.

In the postoperative care, if bony union is not present at the end of five months it is permissible to remove the external immobilization, since the position will not be lost.

An example of the foregoing procedure follows:

A boy, age five, was first seen by me on Sept. 4. 1957. He had developed the signs and symptoms of poliomyelitis on Aug. 24, 1957. Involvement included both shoulders. The left shoulder was operated on April 19, 1960 (fig. 1). The arthrodesis was considered solid on July 19, 1960 (figs. 2A and 2B). Subsequent procedures have included fusion of the opposite shoulder.

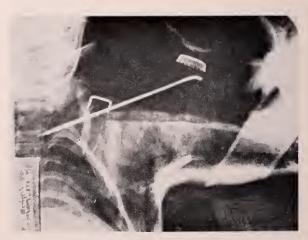
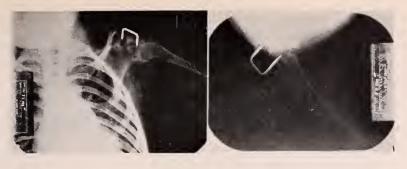


Figure 1

Shoulder fusion in case four weeks postoperative. Note Crowe point pin and staples.



A Figure 2 B

AP and axillary x-rays showing bony union three months postoperative.

# Elbow

Restoration of function at the elbow is related to that of the shoulder, since if the shoulder can be abducted to a point where gravity can be effective to flex the elbow, a flexorplasty is sometimes not necessary. If flexorplasty is done, the modification of Bunnell diminishes the pronatory influence of the transfer<sup>2</sup>. Prior to any surgery at the elbow, careful consideration should be given to the facts that complete extention of the elbow is usually necessary to use crutches, and that flexorplasty almost always results in a flexion contracture.

### **Forearm**

A deformity occasionally encountered in children who have been severely paralyzed by poliomyelitis is a supination contracture of the forearm. This deformity can be corrected by osteoclasis:

A girl, age two months, was stricken with poliomyelitis on July 14, 1952, and came under my care on Aug. 6, 1952.

In May, 1960, the child had good elbow and shoulder function. The forearm was held in com-

plete supination and had some function in this position (figs. 3A and 3B).

On July 1, 1960, an osteoclasis was performed. Full pronation was obtained (figs. 4A and 4B). X-rays made on July 31, 1960, show early callus formation. Films made in October, 1960, reveal reorganization of the bones (figs. 5A and 5B).

This procedure was followed by an opponens transfer and splicing of the distal end of the profundus of the small finger into the profundus of the index finger to augment its flexion.

# Wrist and Hand

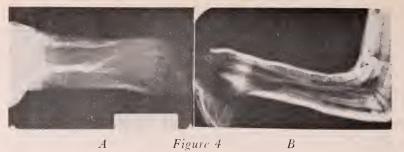
In the forearm, as well as elsewhere in the body, inspection of a muscle that cannot readily be evaluated clinically will at the time of surgery give an idea as to muscle strength. Tendon transfers can be of great use in restoring function about the wrist and in the hand. In the severely paralyzed forearm, wrist, and hand it is wise to delay wrist fusion, since this may preclude the use of tenodesis.

A very common operation is that of opponens transfer. The literature states that one should wait



A Figure 3 B

AP and lateral views of forearm prior to osteoclasis.



X-rays in plaster three weeks after osteoclasis.



Union with remodeling of bone three months postosteoclasis.

until the child is pre-teenage. It has been my experience, however, that opponens transfers can be done successfully as young as the age of seven. I most commonly use the flexor digitorum sublimis of the ring finger as a motor, the flexor carpi ulnaris or a loop of the tendon of this muscle as the pulley, and a subcutaneous passage. Insertion into bone is carried out when extension of the thumb is good; insertion into the extensor apparatus after the method of Riordan<sup>5</sup> is done when extension of the thumb is poor. Appropriate tension of the transfer is most important.

If it is not feasible to carry out tendon transfers, a bone block after the method of Foerster-Thompson can be done<sup>3,6</sup>. A useful point in the technique is to use a small Steinmann pin to hold the thumb in opposition. One should remember that the presence of an osseous bar in the adductor web may preclude the use of crutches or of a wheelchair.

In carrying out tendon tansfers about the hand and wrist, it is important to consider the amplitude of flexors and extensors of the fingers and those of so called wrist tendons: Flexor/extensor/wrist:: 3/2/1.

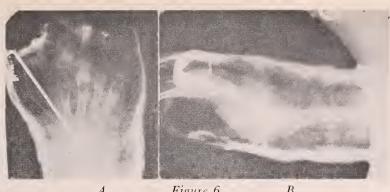
A useful procedure sometimes overlooked is that of tenodesis. In a wrist or hand which has very weak flexion and good extensors, tenodesis of the profundi into the radius and subcutaneous transfer of the extensor pollicis longus to the volar aspect into the ulna can restore a rough grasp.

Wrist fusion can be done and will liberate the wrist tendons for transfer. Since they no longer have to move the wrist, their effective amplitude is greater. The use of a small Steinmann pin across the radiocarpal joint to hold position has been most useful:

A boy, age 16, was first seen in January, 1960, with a palsy of the right hand, probably due to birth injury. A wrist fusion was done on August 9, 1960. X-rays made on August 10, 1960, show the use of a Steinmann pin to hold the wrist fusion (figs. 6A and 6B). Iliac bone was used as a graft. This pin was removed six weeks postoperatively, at which time a long arm cast which was in place was changed to a short arm cast. Fusion was solid at the end of three months (figs. 7A and 7B).

# Summary

Shoulder fusion, osteoclasis of the forearm, opponens transfer, bone block, and wrist fusion are discussed in relationship to the restoration of function in paralyzed upper extremities. The use of a Crowe point pin and a staple in shoulder fusion, various points of technique in opponens transfer, and the use of a transarticular pin in wrist fusion are described and their value delineated.



BFigure 6 AP and lateral views of the wrist immediately after wrist fusion.



Figure 7 Union of wrist fusion three months postoperatively.

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### Postgraduate Meeting in Las Vegas, N. M.

A two-day postgraduate meeting for the diagnosis and treatment of psychiatric cases will be held in Las Vegas, N. M., March 9 and 10, 1962. The Friday session will be at the New Mexico State Hospital and the Saturday meeting at Highlands University.

Speakers will be Dr. Warren Vaughan, Jr., San Mateo, Calif.; Dr. Robert Hewitt, Boulder, Colo., director of WICHE; Dr. Theodore Watters, New Orleans; Dr. William Sheeley, Washington, D. C.; Dr. Thomas Hogshead, Las Vegas, N. M.; Stuart Boyd, Ph.D., Highlands University; and Lester

Libo, Ph.D., Santa Fe.

The meeting was initiated by the Mental Health Committee of the New Mexico Medical Society, headed by Dr. Roy Robertson of Albuquerque, and sponsored by Highlands University, the New Mexico State Hospital, and the American Academy of General Practice, the national Mental Health Committee of which Dr. Leland S. Evans of Las Cruces, N. M., is chairman.

The program is being made possible by a grant from Eli Lilly and Company.

### The Treatment of Premenstrual Tension and

### Dysmenorrhea With a Non-Narcotic Analgesic\*

WILLIAM G. CALDWELL, M.D., \*\* Los Angeles

Frank<sup>1</sup> in 1931 described premenstrual tension and since then the disturbance has been recognized as a clinical entity. In fact, its frequent occurrence places it high on the present-day list of gynecological complaints. Diagnostically, it presents no difficulties because the clinical picture is quite constant, only varying in degree and severity. However, not so well understood are other phases of the problem such as etiology, pathology and treatment.

The condition is seen more often in unmarried women although it is not uncommon in those who are married. It is definitely more common in those who have not borne children. It is supposedly more common in the Caucasian race with Orientals having the lowest rate of incidence. It is more often found in the tense, nervous patient rather than in her more placid sister.

Recent studies indicate that it is seldom a problem of the very active athletic-type girl, particularly swimmers. This would seem to indicate a relationship of its presence to a sedentary-type life. Although it has no specific occupational cause, i.e. it is not an occupational disease, it does have a definite effect on the occupational ability of those sufferers who are employed and in fact has caused a justified concern in industry. Its occurrence, for some unknown reason, has increased during recent years. This may be due to the popularity of the subject given wide exposure by some of the socalled "popular women's magazines."

Unpleasant symptoms of varying degrees are experienced in about two-thirds of normal women from four to seven days prior to the onset of menstruation. These symptoms include headache, breast tenderness, abdominal bloating, generalized

\*Presented during the Bahamas Medical Conference, Nassau, April 30-May 6, 1961. \*\*Department of Clinical Research, St. Anne's Hospital, Los

edema, thigh pain, fatigue, irritability and mental depression. The peak is usually reached before menstruation with a dramatic subsidence of symptoms occurring on the first day of the period. However, many experience symptoms throughout most of the period and according to Griffin<sup>2</sup> these are frequently related to dysmenorrhea.

### Hypotheses

There are several hypotheses regarding the etiology of this condition such as "menstrual toxin," emotional instability, allergy, abnormal sodium retention and excessive fluid retention, hormonal imbalance and thyroid imbalance. Since so many different and divergent possibilities are given as causes, it can be concluded that either the true etiology has yet to be discovered, or - and probably more likely - the condition is due to a number of different causes.

Abundant literature espousing the various theories has caused the average busy physician to approach the problem in a rather hit or miss fashion without giving proper study to the individual's probable etiological factor.

In an effort to give proper consideration to the chief "etiological theories," a brief summary of them is indicated.

### Menstrual Toxin

The possible existence of a menstrual toxin was, perhaps, anticipated more than seventy-five years ago by Jacobi3, who expounded the "menstrual wave" theory, ascribing menstrual molimina to cyclic ebb and flow of somatic functions. Recently, two theories have been adduced regarding the nature of the alleged menotoxin.

The Smiths<sup>4,5</sup> believed that menstrual toxin is of endometrial origin, a product of tissue catabolism during the menstrual cycle. They found the toxin in the euglobulin fraction of menstrual discharge and subsequently demonstrated some of its properties in the circulating blood of women during menstruation, late pregnancy toxemia, and prolonged labor.

The Smiths<sup>4,5</sup> postulate that manifestations of menstrual distress, with the possible exception of mastodynia, are ascribable to local congestion and irritation from the vascular effects of menstrual toxin. Accordingly, they believe that premenstrual tension is attributable to excessive absorption of menstrual toxin from persisting secretory endometrium, the chief source of the disturbing material; and that the dysmenorrhea is the result of uterine colic, arising from the effect of the toxin on the myometrium.

Such a uniform explanation of premenstrual tension and dysmenorrhea would be most welcome, paticularly if it were substantiated by some experimental method. If, for instance, it could be demonstrated that premenstrual tension never occurs in women who have both ovaries but have no uterus (the endometrium of which is the site of formation of menstrual toxin), there would be good reason to accept the menstrual toxin explanation of the multiple symptoms.

In the absence of such experimental proof, it is perhaps significant that menstrual molimina lessen just as soon as shedding of the endometrium and diuresis of menstruation begins, processes which, according to the Smiths, represent the removal and excretion of the toxin. However, whatever the mechanism of its formation and whatever its chemical identity, menstrual toxin could certainly be responsible for premenstrual intoxication of women, and it must be continued to be regarded as an attractive theory.

### Hormonal Imbalance

Disordered metabolism of both estrogen and progesterone, causing secondary effects leading to the symptoms of premenstrual tension, although a popular theory, has not as yet been scientifically proven. Thus, premenstrual symptoms have been ascribed to an excessive quantity of estrogen because of progesterone deficiency (Israel<sup>7</sup>) and upon quite the contrary, an excess of progesterone (Gillman<sup>8</sup>).

It is claimed that the hormonal balance causes an excess of extracellular fluid retention. Thomas<sup>9</sup> has stated that cessation of premenstrual symptoms is concurrent with spontaneous diuresis at the onset of menses. Efforts to accomplish diuresis by using various diuretic agents have not always proved satisfactory, which may indicate that the fluid retention is caused by some factor other than hypernatremia.

A plausible explanation has been a cyclic increase in the pituitary antidiuretic hormone. The mechanism by which the suggested steroidal alterations gives rise to manifestations of premenstrual tension has been attributed to the capacity to evoke retention of the sodium ion, giving rise to excessive fluid in various tissues. Although the pathogenesis of the steroidal imbalance which allegedly leads to the retention of sodium chloride and water is not clear from our present knowledge; the hidden water retention does cause symptomatology in accordance with the organ containing the water.

Another explanation for premenstrual retention of water is by Thomas<sup>10</sup> who hypothecated the existence of a hormone which increases temporarily the antidiuretic action of the posterior lobe of the pituitary. This viewpoint is also shared by Bickers<sup>11</sup> who reported that the symptoms of premenstrual tension could be reproduced in part by daily injection of pitressin during the luteal phase of the menstrual cycle. If proved, this explanation (that of the premenstrual water toxemia being evoked by the presence of an excessive quantity or increased activity of antidiuretic hormone is important from a therapeutic standpoint.

The observations of Morton<sup>12</sup>, an advocate of the "deficient progesterone" pathogenesis of the premenstrual alteration of carbohydrate metabolism (increased sugar tolerance) in some patients, throws a new light on some of the mental and nervous symptoms. Morton's demonstration of hypoglycemia during the premenstruum readily accounts for some of the psychic changes, including the heightened anxiety and fatigue manifest in women suffering from recurrent tension.

That a relationship exists between estrogen levels and carbohydrate tolerance, particularly in diabetics, has been shown by many observers. It has also been pointed out that hypoglycemia results in personality disturbances and fatigue. It is therefore possible, as Morton indicates, that the unopposed action of estrogen premenstrually—unopposed in the absence of sufficient progesterone—results in water retention and hypoglycemia, both of which cause the curious symptomatic combinations of premenstrual tension.

### Psychogenic Disorder

The significance of menstruation cannot be denied, even though its biologic meaning may lie deep in the unconscious. The interpretation, however, of behavior alterations attuned to the menstrual cycle is difficult because of intricately related socio-economic and psychologic factors. The complexity of such relationships in respect to menstruation and reproduction has been reviewed from varied points of view by Deutsch<sup>13</sup>, Ford and Beach<sup>14</sup> and Benedek<sup>15</sup>.

Observing women with severe premenstrual tension one cannot escape the conviction that cyclic changes in the patient's behavior must be based — in some fashion — on unconsciously expressed psychogenic reasons. There are doubtless innumerable psychologic mechanisms, such as unresolved oedipal conflicts and hidden marital discord, which could easily be responsible for some of the clinical patterns of premenstrual tension.

One fairly constant denominator, present in most patients who suffer such menstrual distress, is the association with other functional derangements, such as dyspareunia and indeterminate gastrointestinal symptoms. The latter are found especially in immature individuals, those who are manifestly dependent upon others. Snaith and Ridley<sup>16</sup> consider patients to be "emotionally immature" when their life histories show failure of emancipation either from parents or from precepts and prejudices of adolescence. Their dependency may masquerade behind a façade of apparent aggressiveness but, when exposed, the groping for security may be recognized.

Therefore, even if organic etiology were to be proved for premenstrual tension, there would still remain a complex symptomatic overlay because of the many emotional references universally linked to the phenomenon of menstruation. The prevalence of this condition along familial patterns suggests that there is an undeniable association due to early impressions received from the reactions of mothers or older sisters.

The young girl who repeatedly hears and observes her parent complain of painful symptoms. miseries, etc., month after month, is bound to expect these same symptoms to be a natural occurrence, and so soon falls into the same pattern or syndrome. The wide use of the deplorable synonym "the curse" has caused many young girls to look on this natural monthly occurrence as just that -"a curse" - or blight on her life. Also repeated admonitions regarding the restriction of normal activities during the menstrual time is certain to cause a tendency for an increase of premenstrual symptoms and dysmenorrhea. Is it any wonder that a young girl who is given this false type of indoctrination ends up as a true "inenstrual cripple"?

The fact that many mothers use the menstrual part of the month as an excuse to fall apart completely, or worse yet, as a reason to gain sympathy, cannot help but have a deleterious effect on the young daughter. Indeed it acts as a repeatedly ingrained stimulation for the young girl to fall into the same pattern. Although modern medical education is slowly refuting this teaching, there is vast room for improvement. The present-day increase of women partaking in athletics has done much to prove that the popular though ill-founded restrictions have no basis — medical or otherwise.

Recent studies prove that girls enjoying an active athletic life are singularly devoid of premenstrual tension and dysmenorrhea. Undoubtedly, pelvic motility resulting from athletics plays a big factor in the absence of symptoms.

The term "dysmenorrhea" is a "catch-all" for numerous symptoms associated with the menses, and as such is a symptom complex rather than a disease entity. It is commonly divided into two types — primary and secondary. It is considered primary when it occurs early in menstrual life, and secondary when it appears after a number of symptomfree menstrual years. The etiology is variable and oftentimes very difficult to identify. The most common causes are those associated with pelvic pathology and last, but by far not least, psychosomatic or emotional.

Studies have shown that the average pain threshold to stimuli is lower in dysmenorrheic women and that those suffering from the primary type showed a higher sensitivity to painful stimuli than others. Contractions of the uterus are conveyed to the consciousness of susceptible individuals as pain, whereas these contractions are apparently not received as such in others. The severity of symptoms is very variable in both the primary and secondary types. Many theories are offered regarding the actual cause for the pain experienced none of which is universally accepted. The most popular of these theories, in brief, are as follows.

Moir<sup>17</sup> stated pain was due to an ischemia of the myometrium secondary to contractions. Bickers<sup>11</sup> is of the opinion that abnormal behavior of the muscle is the result of physiological defect in the muscle itself, probably congenital. Taylor<sup>15</sup> considers dysmenorrhea a disorder of the reproductive organs due to circulatory and autonomic imbalance based on psychosomatic factors, which therefore is a disorder of the autonomic nervous system. Many other theories exist, too numerous to mention here. Indeed, the very number of theories leads to utter confusion. It seems obvious that the symptom complex referred to as dysmenorrhea is probably due to several factors and must be assayed on an individual basis.

Although premenstrual tension symptoms are often followed by dysmenorrhea, we must not assume that this is true of all cases. Many patients of the true dysmenorrheic type experience little or no symptoms until the first day of the menses. The true dysmenorrheic patient, especially of the secondary type, should have careful pelvic examinations in order to rule out pelvic pathology. Organic lesions proven to be causative factors are:

Cervical stenosis; Uterine myoma; Septate uterus: Grade 3. fixed, retroverted uterus; Pelvic adhesions; Adnexal varicosities; Ovarian tumors; Endometriosis and adenomyosis.

Time does not permit a discussion of these organic lesions, however, the possibility of dysmenorrhea being due to a specific pelvic lesion must always be kept in mind.

Obviously, the treatment of dysmenorrhea caused by pelvic pathology is the eradication of

the offending lesion. In a previous paper<sup>19</sup> the author discussed the medical management of forty-seven cases of dysmenorrhea with a non-narcotic analgesic\* containing Sandopal<sup>®</sup> (isobuylallyl barbituric acid), caffeine, acetylsalicylic acid and acetophenetidin, especially for the relief of pain, headache and tension states. This discussion deals with this analgesic and sedative in a much larger group of cases for the treatment of premenstrual tension and the symptomatology frequently associated with dysmenorrhea.

Friedman et al.<sup>20</sup>. Blumenthal et al.<sup>21</sup>, Ryan<sup>22</sup>, de Sola Pool et al.<sup>23</sup>, Friedman et al.<sup>24</sup>, and Weisman<sup>25</sup> reported excellent results with Fiorinal<sup>®</sup> in tension headache. Drake<sup>26</sup> reported that this is one of the best sedative-analgesic preparations for the temporary treatment of tension headache. It tends to prevent a mounting build-up of nervous tension and in addition seems to relax the musculature about the head and neck. Easing of the head discomfort is generally accomplished without any unpleasant side effect such as gastric upset.

This series of cases consisted of 127 patients with premenstrual tension and 248 patients with dysmenorrhea. Fifty-three of the premenstrual tension series also suffered with dysmenorrhea, whereas 182 cases of the dysmenorrheic group had little or no premenstrual symptoms. The average age of all patients was 33.4 years. Ninety-four were married and 154 were unmarried. Of the 94 married, 51 had borne one or more children. Twenty-two were known sterility problems.

### Symptoms

Many complaints were common to both the premenstrual and dysmenorrhea group, particularly applicable to the 53 patients of the premenstrual series who also had dysmenorrhea.

The chief symptoms encountered are listed in Table I. Table II shows the types of pelvic pathology encountered.

The frequently maligned uterine suspension operation has been used with very good results when specific indications were present. I mention this at this time since of the eleven cases having a fixed 3° retroversion, nine experienced complete relief of their dysmenorrhea following surgery.

<sup>\*</sup>Known as Fiorinal, marketed by Sandoz Pharmaceuticals.

### Table I

Premenstrual Tension	(128 total)	1
----------------------	-------------	---

Abdominal water retention	.121
Generalized body edema	37
Depression	48
Irritability	69
Fatigue	. 31
Breast tenderness	27
Inability to perform occupational	
duties at par level	78
Restlessness	79
Headaches	93
Nervousness	81

### Dysmenorrhea (248 total)

227
127
48
172
. 131
138
42
62

Note: Most patients in both groups complained of a multiplicity of symptoms.

### Table II

### Types of Pelvic Pathology

Uterine retroversion, grade 3, fixed	11
Cervical stenosis	2
Dermoid tumor of ovary	1
Uterine myoma	4
Adnexal varicosities	2
Endometriosis	3
Adenomyosis	3
Cystic ovarian disease	1
Pelvic adhesions (various causes)	3
Chronic P.I.D.	1
Uterine prolapse	2
Meno-metrorrhagia	4

The rising incidence of endometriosis and its definite association with secondary dysmenorrhea is of particular importance, especially since the condition is so difficult to diagnose preoperatively. However, I do not wish to infer that an exploratory laparotomy on every dysmenorrheic patient is recommended.

Dysmenorrhea often continues to plague the patient, even after removal of the gross pathology which the gynecological surgeon inadvertently assured the patient was the cause of her symptoms. Thus, as one "who has been there," extreme caution must be exercised in offering promises of relief on the basis of surgical correction. It is a human error considered to be the occupational hazard of the gynecologist.

In the combined series studied most of the patients had tried various forms of medication for the relief of symptoms with mostly poor results. Many complained because of severe side effects — severe enough to cause disuse, even with relief of symptoms. Some had even been subjected to such severe "pain killers" as Percodan®\* and other related narcotics. A very hazardous type of treatment, to put it mildly. Most commonly used were the analgesic-amphetamine compounds. A few patients admitted taking alcoholic-type patent medicine, claiming "glowing" results.

### Dosage

Although there was a wide variation of dosage in the series studied, best results with Fiorinal® were noted when an initial dose of two tablets was given at the first onset of complaints. This single initial dose proved effective in causing a cessation of symptoms in many cases, particularly those complaining of tension headache. Several cases with more severe symptoms required subsequent medication of two tablets each at four-hour intervals before relief was noted.

Others had definite diminution of symptoms so that subsequent doses of one tablet at four-hour intervals proved sufficient. Due to the complete absence of side effects a wide choice of dosage schedule was possible, based on individual needs. With proper education of the patient in recognizing the first symptoms of pain or discomfort, so that she would take the initial dose of two tablets at the first signs of discomfort, self-reduction of medication was possible.

The premenstrual group were cautioned regarding salt intake, and 78 of them were given a prophylactic diuretic starting with the first evidence of abdominal water retention which was observed to occur usually on the fifth and sixth day before the onset of menses.

<sup>\*</sup>Endo Laboratories

The wide margin of safety of Fiorinal permitted dosage intake varying from a minimum of one tablet to several cases of the severe dysmenorrheic class, who required a total dosage of 12 tablets over a two-day period. The average dose for all cases studied was between four and six tablets.

### Results

For purposes of evaluation the total number of cases observed (248) was broken down into three classes, based on the severity of symptoms (see Table III).

T. I.I. TIT

Table III				
Very severe 54	Severe 138		2.20	lerate 56
Results	Excellent	Good	Fair	None
Very severe	10	25	11	8
Severe	71	32	30	5
Moderate	51	5		

### Discussion

The apparent increased incidence of a complex disabling condition referred to as dysmenorrhea poses a perplexing problem, due to the confusion that exists as to its cause. It is this confusion regarding "causative factors" that has resulted in treatment of this condition being a hit or miss affair.

It is evident from this series of 248 cases studied that there are undoubtedly several probable causes for the presence of both premenstrual and dysmenorrheic symptoms. Thus, each patient must be studied individually and treated accordingly. The presence of pelvic pathology required specific correction. Unfortunately, many practicing physicians approach the problem with a sense of hopelessness and as a result miss a very specific etiological factor.

To say these conditions are so common that they should be considered as a common occurrence of the psychosomatic female is a human tendency, although erroneous. Casually prescribing potent "pain killers" — even narcotic derivatives, is very dangerous and does not solve the problem. In this series (248) of widely divergent cases very satisfactory results were obtained with a non-narcotic analgesic.

The total absence of side effects in a representative series is noteworthy. So many medications used in treating this condition defeat their purpose by causing side effects often more debilitating than the original symptoms. This factor is of great importance in enabling the more severely affected patients to carry on with their regular duties. Education and encouragement of the patient are important aspects of any treatment. Reassuring the patient that the medication used will not cause dependency is of unquestionable value.

### Summary

- 1. Two hundred and forty-eight private patients between the ages of 16 and 48, with an average of 33.4 years, whose symptoms were those of premenstrual tension or dysmenorrhea, are reported.
- 2. Forty-two cases of the series had pelvic pathology, of which 21 received surgical treat-
- 3. Fifty-three patients suffered from both premenstrual tension and dysmenorrhea.
- 4. One hundred and fifty-four were unmarried, 94 were married, 51 having borne one or more children.
- 5. An initial dose of two Fiorinal® tablets, taken at the first sign of symptoms and followed at four-hour intervals with one or two tablets, proved the most efficient dosage schedule.
- 6. Dosage requirements varied from a minimum of one tablet to a maximum of 12 tablets, given over a two-day period. The overall average dosage for the series was between four and six tablets.
- 7. Individualization permitted a reduction of dosage in 137 cases.
- 8. No side effects were noted in any of the 248 cases.
- 9. One hundred and ninety-four cases whose symptoms varied from very severe to moderate, raceived excellent to good results.

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### Writing Awards Contest

Judges in Southwestern Medicine's \$500 best article contest will be selected by American Medical Writers' Association and will be members of that Association. There will be at least three judges, Dr. Richard H. Orr, president, has announced.

Last month it was announced a total of Five Hundred (\$500.00) Dollars will be awarded annually for the best original scientific articles to be published in *Southwestern Medicine* starting with the issue of January 1962.

### Contest Rules

Original scientific articles published in South-western Medicine will be eligible.

Awards will be made in two classifications: Regional and National. All physicians who practice in West Texas, Arizona. New Mexico, Nevada, or Northern Mexico (States of Sonora and Chihuahua) will be eligible to compete for the regional awards. All physicians in the United States outside the regional area may compete for the national awards.

Awards will be made in the following amounts:

Regional; One hundred dollars for the best paper, seventy-five dollars for the second best paper. and fifty dollars for the third best paper.

National; One hundred dollars for the best paper, seventy-five dollars for the second best paper, and fifty dollars for the third best paper.

The contest for 1962 will close on Sept. 1, 1962.

Contributions must be written in English, typed, double spaced on one side of paper only. A stamped, self-addressed envelope must accompany each paper to insure return of rejected manuscripts.

Papers should be submitted to Lester C. Feener, M.D., Editor, 310 North Stanton Street, El Paso, Texas, by July 1 for judging in the 1962 contest.

Only papers acceptable to the board of editors of *Southwestern Medicine* will be published.

### APHORISMS and MEMORABILIA

Edited by Andrew M. Babey, M.D., Las Cruces, N M

### Miscellaneous Truths and Concepts

- 1. "Physical courage is admired by every one, hence it is universal (soldiers are by definition brave even in a conscripted army): moral courage is admired by few, so it is rare: intellectual courage is admired by no one, consequently it does not exist." Trotter, W.: Instincts of the Herd in Peace and War, London, Unwin, 1916, 213 pp. as quoted by William B. Bean, Archives of Internal Medicine, Vol. 106, Nov. 1960 pp.212/734
- "Clinical signs of atherosclerosis appear only after ulceration and calcification of the cholesterol accumulations within the arterial walls have taken place, and such cases are advanced far beyond the stage of mere cholesterol deposition. Increasing linolenic acid and decreasing cholesterol intake after calcification of atheromatous plaques has set in resembles closing the barn door after the horse has been stolen. After all, the middle-aged man threatened by compulsory retirement, harassed by "scientific" reports distributed daily by radio and television reminding him that he has reached the age of carcinoma development, saddened by the decrease of certain highly important functions and discouraged by the development of the many other indignities inherent to middle-age, is left with only a few of the pleasures he once upon a time savored to the full. It is true that we are digging our graves with our teeth but to stop this dearly enjoyed habit after 50 or 60 years seems a high price to pay for an unlikely cure of well-established arteriosclerosis." I. Shapper, M. D., "Bedside Medicine," Grune & Stratton, New York, 1960 pp.36
- 3. "Only too often the abdominal aneurysm bursts after palpation. Once the diagnosis of an abdominal aneurysm has been made, the patient should be warned against inquisitive

- physicians. This preventive measure usually considerably prolongs the life of these patients. The dangers of palpation are well illustrated by the experience that a postgraduate course in cardiology usually markedly increases the fatalities among patients with abdominal aneurysms admitted to the hospital where the course is given." ibid. pp.37-38
- 4. "It is often forgotten that after the hemorrhage has stopped, the hemoglobin continues to decrease for the next two or three days. This is due to dilution of the circulating blood by the tissue fluid which flows into the blood in order to keep the volume of the circulating blood near normal values. Thus, if blood transfusions are ordered because the hemoglobin decreases during the first days after the hemorrhage has stopped, the ensuing excessive increase of the circulating blood volume may cause the hemorrhage to recur. In other words, for the treatment of a hemorrhage, pulse, blood pressure. weakness and perspiration are better criteria than the hemoglobin determination and ervthrocyte count." ibid. pp.101
- 5. "Renal involvement in systemic lupus erythematosus is the least responsive of all the clinical manifestations of the disease. Our study demonstrated that amounts of corticotropin or glucogenic steroids sufficient to suppress the other manifestations of systemic lupus erythematosus had no effect either on the prevention or the amelioration of renal damage." Louis Soffer, Louis Southern, H. E. Weiner, and R. L. Wolf, "Annals of Internal Medicine." pp.215, Feb. 1961
- 6. "In other words, much of the work that is being done and the papers that are being published are done and published for the wrong

reasons: because someone had too much money to spend; or because a government official had to dispose of all the appropriated funds within the fiscal year; or because someone forced someone else to work in an area not of his own choosing; or because someone found it easier to drift along on fellowships than to strike off on his own; or because a practitioner thought it would 'look good' if he did some research; or because an assistant professor needed 'to publish' to get a promotion; or because of a thousand other reasons irrelevant to the advancement of medical knowledge. Shoddy reasons for doing research tend to produce shoddy research." - John M. Russell, president of the Markle Foundation, in the Foundation's report for 1959-60, p.2 as quoted in "The Lancet" May 6, 1961, p.991

7. "For a few sensitive souls a grammatical blunder produces a physical effect like being hit in the midriff by a not quite spent bullet. Such errors they may forgive but cannot forget. This state of linguistic hypersensitivity makes one's

life miserable as one wades around through atrociously written medical articles, becoming engulfed in quicksands of cliches, jargon, and pseudosophisticated nonsense. But at least this sensitivity does have the merit of making the search for excellent medical writing or good speakers doubly rewarding whenever a gem is found." — William B. Bean, M.D., Arch. Int. Med., "Tower of Babel 1961," Vol. 108, July 1961, p.5

8. "In the final analysis, when evaluating the risk, I am concerned most with the patient's ability to do physical exercise. Is he living an active, normal life? If a man of 70 or 80 works around the house, goes up and down stairs without difficulty, perhaps mows the lawn and takes long walks, or if an elderly woman does ordinary household chores, such patients usually can tolerate the stress of a major surgical procedure. They have already proven themselves by living a long life." — C. E. Sedgwick, M.D., The Lahey Clinic Bulletin, Vol. 12, No. 3, Jan.-Mar., 1961, p.82

### New Mexico News . . .

Dr. Jack Redman of Albuquerque has filed in the New Mexico Republican primary on May 8 for U. S. Congressman. Contributions to his campaign may be addressed to Redman for Congress Committee, 2518 Central, S.E., Albuquerque. N. M.

\* \* \* \* \*

The Federation of State Board of Medical Examiners with headquarters in Chicago has appointed a new editor of its bulletin, Dr. R. C. Derbyshire, Santa Fe, President-Elect of the New Mexico Medical Society.

\* \* \* \* \*

Because the University of New Mexico School of Medicine in Albuquerque, N. M., is not yet eligible for approval by the appropriate councils of the American Medical Association and the Association of American Medical Colleges, it cannot at this point receive the support accorded approved medical schools by the AMEF.

Although the school is still in a developing

state, it already has a need for unrestricted funds, and this need will increase dramatically with the growth of the school. A separate agency account designated "Medical School, Unrestricted Funds" has been established by the University Comptroller as a receiving and operating account to meet this need. This account will provide essentially the same function for the new school as is generally provided by AMEF funds, and indeed will be desirable as a supplement to AMEF support when the latter becomes available.

Contributions to this account not only will be gratefully appreciated but are urgently needed. Flexibility in the ability to provide interim support for the new faculty members as the latter are selected will undoubtedly make a critical difference in the quality and degree of excellence of the school itself.

Contributions may be made directly to "University of New Mexico School of Medicine," Albuquerque, N. M., Dr. Reginald H. Fitz, Dean, has announced.



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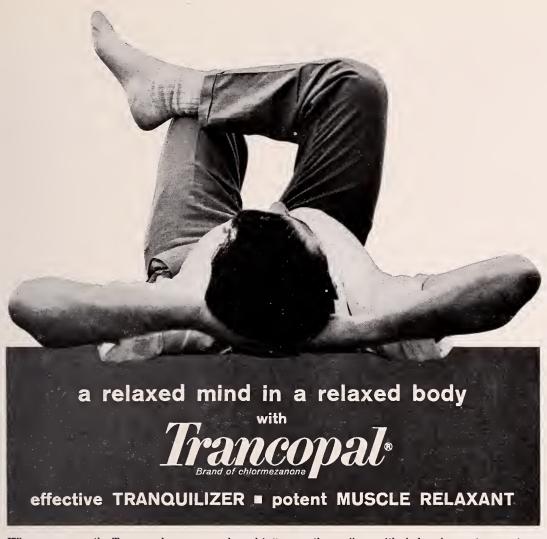
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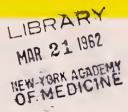
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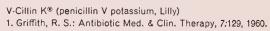
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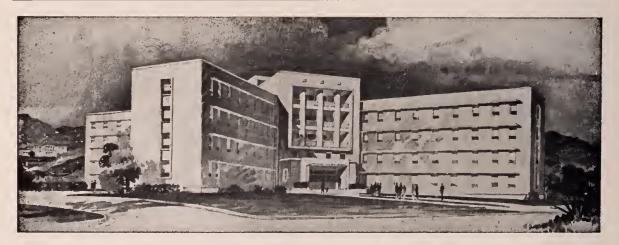
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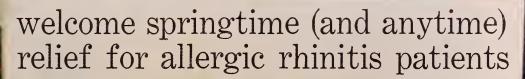
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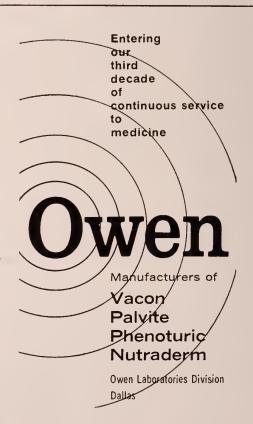
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### Coming Meetings

Southwestern Surgical Congress, annual meeting, Western Skies Hotel, Albuquerque, Apr. 2-5, 1962.

United States - Mexico Border Public Health Association, annual meeting, Nuevo Laredo, Tamaulipas, Mexico. Apr. 9-12, 1962.

University of Texas Postgraduate School of Medicine, El Paso Division, Postgraduate Course, El Paso County Medical Society Turner Home, 1301 Montana Avenue, El Paso, Apr. 15, 1962.

Bernalillo County Heart Association, Cardiovascular Institute, Civic Auditorium, Albuquerque, Apr. 26, 27, 1962.

New Mexico Medical Society, annual meeting,

Hobbs High School, Hobbs, N. M., May 8-11, 1962.

Texas Chapter, American College of Chest Physicians, annual meeting, Municipal Auditorium, Austin, May 13, 1962.

The Western Association of Railway Surgeons, annual meeting, Stockmen's Motor Hotel, Elko, Nev., Sept. 27-29, 1962.

Southwest Obstetrical and Gynecological Society, 12th Annual Meeting, Camelback Inn. Phoenix. Oct. 10-13, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.



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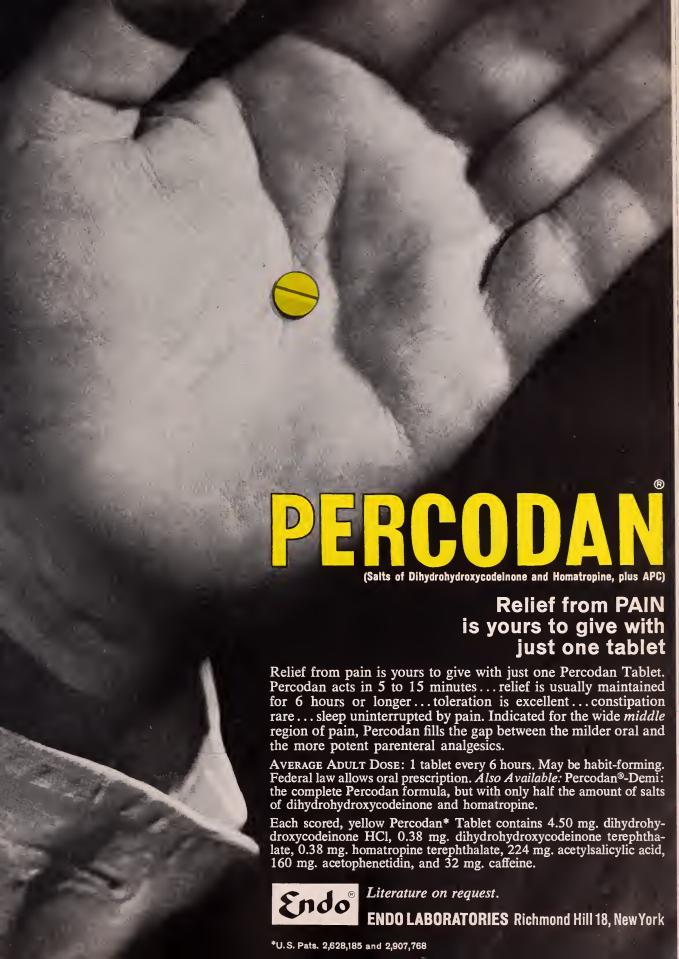
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# MEETINGS



Dr. Black

### Dr. Gordon L. Black Elected President of

### Texas District One Medical Association

Dr. Gordon L. Black of El Paso was elected president of District One of the Texas Medical Association in Pecos, Texas, February 3.

Other new officers are Dr. Charles Jones. Fort Stockton, vice-president; Dr. William Gaddis, El Paso, secretary-treasurer; and Dr. Charles E. Oswalt, Jr., Fort Stockton, counselor. Retiring president is Dr. Harold Lindley of Pecos.

Principal speaker at the annual meeting was President of the Texas Medical Association, Dr. Harvey Renger of Hallettsville, Texas.

Born in Pecos, Dr. Black received his B.A. from the Texas College of Mines and his M.D. from the University of Texas Medical Branch in Galveston. He interned at Philadelphia General Hospital and then took a three-year residency in Radiology at the University of Rochester Medical School's Strong Memorial Hospital.

Dr. Black came to El Paso in 1948 and became associated with the offices of Drs. Mason, Hart

and Boverie, now Drs. Hart, Boverie, Black. Clayton, Green and White.

He is certified by the American Board of Radiology, a past president of the Southwestern Radiological Society, secretary-treasurer for four years for the District One organization, a past secretary-treasurer of El Paso County Medical Society and a past program chairman for two years for the El Paso society.

He is a director of the Breakfast Optimist Club, a member of the board of directors of Boys Baseball of El Paso, Inc., and an elder in the Meneeley Presbyterian Church. He and his wife reside at 3025 Aurora Avenue with their two sons and two daughters.

Speakers at the meeting, other than Dr. Renger. were Dr. J. O. Dampeer, Kermit; Dr. E. S. Crossett, El Paso; Dr. James Morgan, El Paso; Dr. Joseph Lucci, Houston; Dr. M. S. Hart, El Paso; Dr. Edward Downs, El Paso; and Dr. Oswalt, Fort Stockton.

# United States—Mexico Border Public Health Association to Meet in Nuevo Laredo

The Twentieth Annual Meeting of the United States-Mexico Border Public Health Association will be held April 9-12, 1962, in Nuevo Laredo, Tamaulipas, Mexico.

National and state health officials of both U. S. and Mexico will participate in the Inaugural Session. Plenary Sessions will be held during the next three days, each dealing with a single topic of general interest, such as "Integrated Health Program," "Development of Water Supplies" and "Virus Infections."

Dr. Stanley J. Leland, Santa Fe, president of the association and director of the New Mexico Department of Public Health, has announced the following speakers:

Dr. James E. Peavy, Austin, Commissioner of Health, Texas State Department of Health; Dr. Felipe Garcia Sanchez, Director General de Servicios de Salud en Estados y Territorios; Dr. Guillermo Soberanes M., Jefe, Servicios Coordinados de Salubridad y Asistencia del Estado de Sonora; Dr. Eduardo Takasita Elizondo, Director, Centro de Salud de Nuevo Laredo; Eng. Wesley Gilbertson. Washington, D. C., Chief, Division of Engineering Service, U. S. Public Health Service; Ing. Alfredo Colin Varela, Mexico, D. F., Subsecretario, Secretaria de Recursos Hidraulicos:

Ing. Luis Coq, Mexico, D. F., Director, Comision de Construccion, Secretaria de Salubridad y Asistencia; Sr. Antonio J. Bermudez, Mexico. D. F., Director General, Programa Nacional Fronterizo; Dr. Hernan Duran, Washington, D. C., Pan American Sanitary Bureau; Eng. Harold R. Shipman, Washington, D. C., Pan American Sanitary Bureau; Ing. David Herrera Jordan, Ciudad Juarez, Comisionado, Comision Internacional de Limites y Aguas; Col. L. H. Hewitt, El Paso. Commissioner, International Boundary and Water Commission; and Dr. Carlos Campillo Saenz, Mexico, D. F., Director, Instituto Nacional de Virologia.

### Southwestern Surgical Congress to Meet in Albuquerque

The annual meeting of the Southwestern Surgical Congress will be held for the first time in New Mexico, April 2-5, 1962, in Albuquerque with headquarters at the Western Skies Hotel.

Guest speakers for the 14th annual session of the Congress will be Dr. Paul R. Lipscomb, Orthopedic Section, Mayo Clinic; Dr. Chester Mc-Vay, Professor of Surgery, University of South Dakota; Dr. Earl J. Boehme, Assistant Professor of Surgery, Medical Evangelist School, Los Angeles; and Dr. John Stehlin, Jr., Assistant Professor of Surgery, M. D. Anderson Hospital at Houston.

Dr. Lipscomb will speak on "Unsolved Problems of Tendons, Ligaments and Fascia" and "Management of Fractures of Hand and Wrist." Dr. McVay will speak on "Inguinal Hernioplasty" and "Abdominal Incision—A Philosophy." Dr. Boehme will deliver papers on carcinoma of the

colon and thyroid disease. Dr. Stehlin will deliver two papers on perfusion techniques and perfusion drugs.

Outstanding panels will be presented on gastrointestinal disease, traumatic problems and the management of some common neoplasms. Other members of the Congress will present papers on diversely interesting topics.

Officers of the Congress are Dr. Charles M. O'Leary, Oklahoma City, president; Dr. Edgar J. Poth, University of Texas Medical Branch at Galveston, president-elect; Dr. Eugene M. Bricker, St. Louis, Mo., vice-president; and Dr. Robert B. Howard, Oklahoma City, secretary-treasurer. Dr. William R. Coppinger, Denver, is chairman of the Program Committee and Dr. Rodger E. MacQuigg, Albuquerque, is Councilor for New Mexico.

# ORIGINAL ARTICLES

# Obscure Causes of Intractable Cardiac Failure

THOMAS M. RUNGE, M.D., F.A.C.P., Austin

While many cases of cardiac decompensation can be treated successfully without establishing an etiologic diagnosis, in others a specific diagnosis must be made to accomplish a successful outcome. Prominent in this category are myocarditis, particularly rheumatic myocarditis, subacute bacterial endocarditis, decompensation complicating myxedema, cardiac tamponade and constrictive pericarditis, primary cardiac neoplasm, and silent pulmonary embolization, as well as failure complicated by electrolyte disturbances, principally potassium and chloride deficit induced by diversis.

Cardiac decompensation itself is fairly easily recognized and ordinarily responds to routine therapy—that is, rest, digitalization, sodium restriction and diuretics. On the other hand about five to ten per cent of cases do not respond to such measures alone, and in these some obscure factor usually is present causing intractable failure. For this reason it is important to establish not only the fact that the patient is in failure, but also to determine the precise etiology.

The commonest causes of cardiac decompensation are: 1. hypertension. 2. coronary insufficiency with myocardial fibrosis, and 3. valvular disease.

The first two produce left heart failure initially with dyspnea as a prominent symptom, and later right failure<sup>1</sup> is added with peripheral edema and hepatomegaly. Valvular disease may present as left ventricular failure (aortic stenosis or aortic insufficiency) or as right failure (mitral stenosis) or as combined right and left failure (mitral stenosis and insufficiency).

These three common etiologic categories respond to routine measures mentioned above. But

the difficult cases are the five to ten per cent with obscure factors, as follows:

#### 1. Myocarditis

Myocarditis may be the cause of cardiac decompensation and is usually due to active rheumatic fever.<sup>2</sup> Diphtheria, influenza, and other viruses, pneumonia, typhoid fever, rickettsia, mycoses, protozoa, and the obscure Fiedler's myocarditis are rarer causes.

The patient with rheumatic myocarditis often has valvular disease and it is all too easy to assume that cardiac decompensation is on the latter basis alone; with absence of response to the usual measures for failure, it may be felt that an intractable state of cardiac decompensation has been reached. However, smoldering rheumatic fever with myocarditis may be present and may respond to a full therapeutic course of antibiotics to eradicate the provocative beta-hemolytic streptococcal infection.

An illustrative case follows: This 37 year white male (Illustration #1) with intractable cardiac



Figure 1
L.M. 37 year male with rheumatic myocarditis.

decompensation not responsive to digitalization, sodium restriction and rest, was known to have rheumatic mitral valvular disease.

Subacute bacterial endocarditis and pulmonary embolization were both considered but neither proved. Active rheumatic myocarditis was suspected because of poor response to anti-failure therapy and he was placed on a therapeutic course of tetracycline for approximately two weeks. Subsequently he began to improve and was able to return to his job as a ward attendant.

Two years later he again developed intractable failure, at this time associated with hemoptysis and pleuritic type pain in the right lower chest associated with an infiltration in the right lung base. His mechanism at this time was auricular fibrillation and pulmonary embolization was felt probable. He was placed on anticoagulant therapy and bed rest and again became free of edema, cyanosis and venous distention, but remained dyspneic on exertion. Subsequently cardiac catheterization revealed predominant mitral insufficiency. He is now ambulatory on digitalis, anticoagulants and bicillin.

#### 2. Subacute bacterial endocarditis.

Subacute bacterial endocarditis<sup>3</sup> may be an obscure cause of cardiac decompensation, particular-



Figure 2
W.R. 81 year male with subacute bacterial endocarditis.

ly in the elderly where it often presents very little fever, but often anemia and cardiac decompensation which responds poorly to digitalis, sodium restriction and to rest.

An illustrative case follows: This 81 year male (Illustration #2) was hospitalized in intractable cardiac decompensation with anemia and very low grade fever, associated with a harsh grade two systolic aortic murmur. He was found to have subacute bacterial endocarditis, the organism being penicillin sensitive streptococcus faecalis. He was given aqueous penicillin, 40 million units daily plus streptomycin ½ gm twice daily for six weeks. On this program signs of cardiac decompensation cleared despite the fact that he had not responded previously to usual measures including digitalization.

#### 3. Myxedema

Myxedema<sup>4</sup> may present as cardiac decompensation and will not respond to digitalis and other measures unless thyroid extract is added, beginning in small dosage, ½th grain daily, increasing at two weekly intervals until optimal dosage is attained, usually two to three grains per day. This entity is easily recognized once thought of, but



Figure 3
G.R. 69 year female with hypertension and myxedema.

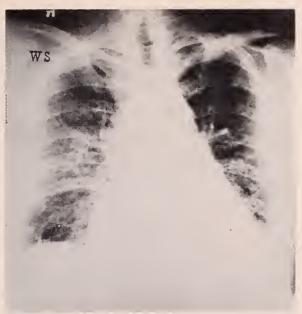


Figure 4
W.S. 58 year male with cardiac tamponade.

in the edematous, dyspneic patient it is easy to overlook the marked thinning of the brows, the myxedematous facies, the elevated serum cholesterol and perhaps a depressed protein bound iodine or iodine 131 uptake.

An illustrative case follows: This 69 year hypertensive female (Illustration #3) was in intractable cardiac decompensation unresponsive to usual measures, but her hypertensive disease was complicated by myxedema. She was cautiously started on thyroid and this gradually increased to two grains over a nine months period. Her failure improved and she survived two more years, finally dying in intractable failure. At necropsy she was found to have no thyroid tissue. The cause of her hypertension was a stenotic renal artery.

#### 4. Cardiac tamponade

Cardiac tamponade is easily recognized once suspected, but only then. The patient is deeply cyanotic with markedly distended peripheral venous system and markedly paradoxical pulse. This can be detected by palpating the femoral arteries which in severe cases may disappear completely during inspiration. It is also detected in obtaining the blood pressure with a mercury manometer, but minor variations in auscultatory threshold of 10 mm should be disregarded.

An illustrative case follows: This 58 year male was hospitalized with severe dyspnea, cyanosis, marked venous engorgement in the neck, and was found to be pulseless, with unobtainable blood pressure. He gave a history of nine days duration of hoarseness, substernal pain of three days duration and onset of dyspnea and syncope 48 hours previously plus nausea. He had an enlarged cardiac silhouette (Illustration #4) and an electrocardiogram showing moderate reduction of voltage, but no other significant abnormalities. Pericardial aspiration revealed 400 cc of apparent blood. This fluid was found to contain 6 gms of hemoglobin and numerous malignant epithelial cells.

He obtained immediate relief from the pericardiocentesis, but succumbed after several months. At necropsy bronchogenic carcinoma with metastases to the pericardium were found.

Constrictive pericarditis<sup>5</sup> presents an identical picture, slower in progression.

#### 5. Cardiac tumor

Neoplasm of the heart can be very confusing. Such a case is illustrated below:

This 73 year white female was admitted to the hospital in cardiac decompensation with paroxysmal auricular fibrillation and left bundle branch



Figure 5

A.S. 73 year female with mesothelioma of Tawara's node.

block. (Illustration #5). She was converted to normal sinus rhythm and failure improved, but in spite of this she had a gradually progressive downhill course and expired in six weeks. Necropsy revealed a primary cardiac malignancy, a mesothelioma originating in Tawara's node. This tumor varied from 2 cm in thickness in the interatrial septum to a few millimeters where it extended into the root of the great vessels and narrowed the lumen of the superior vena cava. It surrounded the coronary arteries. The ventricles showed moderate dilatation with flattening of the trabeculae, but the ventricular myocardium was free from gross alteration.

Rare cases of myxoma<sup>6</sup>, particularly of the left atrium, have been reported, with cardiac failure and with murmurs and clinical signs suggesting mitral stenosis. It is in the hope of finding one of these that the possibility of cardiac neoplasm should be considered when the cause of cardiac decompensation is not clear.

#### 6. Paroxysmal mechanism disorders

Paroxysmal mechanism disorders,<sup>7</sup> particularly paroxysmal atrial fibrillation, which is relatively common in the middle aged and elderly, may be the cause of obscure cardiac decompensation. The patient may report episodes of minutes to hours

or longer duration of dyspnea and may or may not be conscious of rapid irregular heart action.

The treatment of choice is quinidinization if the patient is observed during a free period. However, if the patient presents with the mechanism disorder, digitalization is safer and often results in conversion to normal sinus rhythm, whereupon quinidine can be instituted. During the period of digitalization anticoagulant therapy with heparin is advisable to decrease the likelihood of embolization which may accompany conversion to normal sinus rhythm.

#### 7. Thyrotoxicosis

Thyrotoxycosis<sup>8</sup> may be obscure and may be the deciding factor in maintaining a patient in congestive failure who would otherwise respond to digitalis. The clinical diagnosis is confirmed by the  $I_{131}$  uptake and protein bound iodine. It is often the cause of mechanism disorders including auricular fibrillation and we have seen it produce supraventricular tachycardia with block.

For the patient in cardiac decompensation complicated by thyrotoxicosis the treatment of choice is either antithyroid drugs such as methimazole or propylthiouracil or radio-iodine<sup>9</sup> depending on the patient's age primarily, the latter treatment being reserved for older patients because of the unsettled status regarding neoplastic tendencies of this therapy. If drug therapy is used, subsequent thyroidectomy can be accomplished during a euthyroid and compensated state.

#### 8. Silent myocardial infarction

Some patients, particularly the dark skinned races, rather commonly have myocardial infarction without pain, 10 recognized readily when an electrocardiogram is obtained.

#### 9 Obscure valvular disease

Aortic stenosis in particular may present little or no murmur in advanced cases of failure and coarctation of the aorta with hypertension and failure may be overlooked.

#### 10. Silent pulmonary embolization

Silent pulmonary embolization<sup>11</sup> is particularly likely to occur in the bedridden patient and is often overlooked. Chest films frequently give no

aid and in the patient with cyanosis, and intractable right failure, 12 this diagnosis should be considered and after other causes are excluded the patient placed on long term anticoagulant therapy.

A number of other rare causes of cardiac decompensation are known, Metabolic disorders<sup>13,14</sup> including the xanthomatoses, carcinoid syndrome, glycogenosis, and amyloidosis may be causative. Collagen disorders including polyarteritis nodosa, scleroderma,<sup>15</sup> dermatomyositis, and disseminated lupus erythematosus are occasionally seen. Endocrine abnormalities such as Cushing's syndrome, acromegaly, Addison's disease and familial periodic paralysis may be etiologic factors. Hereditofamilial disorders including muscular dystrophy<sup>16</sup> and Friedreich's ataxia<sup>17</sup> may be causative.

Trauma such as the steering-wheel crush injury, with direct contusion of the myocardium may cause cardiac failure. Avitaminosis such as in beri-beri, peripheral arterial venous aneurysm, Paget's disease (by producing multiple function arteriovenous shunts), and hypoplasia of the aorta may result in intractable failure. The latter is interesting, for although a congenital defect, it is not associated with cyanosis or a murmur and usually presents as painless cardiac decompensation. A rare cause is pheochromocytoma.

Potassium or chloride deficit, usually induced by diuresis with mercurials or other agents, may result in a state of intractable failure.

#### Summary

Most cases of cardiac decompensation are easily recognized as to etiology and establishment of etiology in each case is important, since a successful outcome may hinge on a definitive diagnosis. In many intractable failure cases digitalization, sodium restriction, rest and diuresis are not sufficient and specific therapy for the underlying cause must be instituted if the outcome is to be successful.

Included in this category are myocarditis, usually rheumatic in origin, subacute bacterial endocarditis, myxedema, cardiac tamponade and constrictive pericarditis, cardiac neoplasm, paroxysmal mechanism disorders, thyrotoxicosis, silent myocardial infarction, silent pulmonary embolization, as well as a number of rarer disorders.

The refractory failure patient may also be suffering from chloride or potassium deficit, usually induced by diuresis, and often correction of this deficit will turn the tide toward a favorable outcome in an otherwise discouraging case.

#### 18 Medical Arts Square

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### Traumatic Rupture of Double Kidney\*

ROBERT F. THOMPSON, M.D., F.A.C.S., El Paso

The rarity of this condition makes it of interest. A search of the literature fails to disclose a reported instance of a similar case.

This patient, a male, age 49, fell from a scaffold across a ladder on the ground and was severely injured. He was taken at once to the hospital in one of the neighboring cities and, presenting a surgical abdomen, was operated upon immediately. He was found to have a ruptured pancreas and torn omentum. The convalescence from this operation was uneventful except that marked hypertension with very severe headaches and visional disturbances appeared before he left the hospital. The hypertension was so severe that retinal hemorrhages occurred and the vision was greatly impaired. Transient blindness was present on one occasion.

Two months after the accident he was brought to El Paso for study concerning the headaches and visional disturbances. Complete neurological examination concerning suspected intra-cranial pathology or injury was unremarkable. During the work-up an intravenous pyelogram was made which disclosed a calculus in the right kidney and a staghorn calculus in the left kidney with loss of function in the left kidney. At this point I was asked to see this patient.

#### Duplex Kidney

Complete urological investigation with retrograde pyelography disclosed a calculus in the middle calyx of the right kidney. This kidney had good function. The left kidney was a duplex kidney with two complete ureters which merged into

one common ureteral orifice at the bladder. The upper segment of this kidney was completely filled with staghorn calculus. The pyelography study further indicated that the duplex kidney had been ruptured at the time of the accident as there was evidence of some extravasation of the opaque media. This duplex left kidney was completely functionless. Exquisite tenderness was present in the left flank.



Retrograde pyelogram showing duplex left kidney with two ureters. The upper segment contains a staghorn calculus. Extravasation of opaque media is observed, as is the calculus in the right kidney.

<sup>\*</sup>Prepared for American Urological Association, South Central Section, Hot Springs, Ark.

Operation was performed under spinal anesthesia. A huge, walled-off, perinephritic abscess formation was found in the left loin. An enormous amount of purulent urine was evacuated. This very unusual, ruptured, double kidney was now removed. The blood supply to this kidney was extremely abnormal, also. The nephrectomy was very difficult.

#### Convalescence

Following the nephrectomy the convalescence was satisfactory and uneventful except that the wound drained for a long period of time. The

blood pressure immediately returned to normal with a complete disappearance of the headaches and visional disturbances.

Two months after the operation he visited the office. At that time he had returned to work and was feeling fine. There were no symptoms and the urine was clear.

Nine months later, the calculus in the right solitary kidney dislodged and became impacted in the upper ureter. It was immediately removed by ureterolithotomy. At the present time he is enjoying good health with normal blood pressure. 1900 North Oregon Street

#### Dr. Torrens Heads Bernalillo County Medical Association

Dr. John K. Torrens has been installed as president of the Bernalillo County Medical Association in Albuquerque for the 1962 year.

Other new officers are Dr. J. A. Dillahunt, first

vice-president; Dr. Donald V. Mabry, second vice-president; and Dr. William F. Bank, secretary-treasurer. New members of the board of governors are Drs. Stuart W. Adler, Fred Hanold and C. M. Kemper.

#### British Health Service

Dr. James Hendrick and his wife have returned to Albuquerque after having spent several months in England personally viewing the British Health Service. Dr. and Mrs. Hendrick gathered much information that has not found its way into the press.

The Doctor and his wife are available to discuss

their findings before your Society, Auxiliary, or to any lay group through County Society request. They desire to present their findings to as many people as possible.

Write to Dr. Hendrick at 716 Palomas, N.E., Albuquerque, N.M.

## The Results of Exposure to Solar Radiation

and the Effectiveness
of a Sunscreen Preparation
Under Natural Conditions

EDMUND F. FINNERTY, M.D.,\* Boston

Knowledge concerning the effects of solar radiation on human skin has increased in recent years. That the ultraviolet radiation emitted is absorbed by the skin, and that the natural consequence can be a painful and perhaps serious burn, are facts only too vividly implanted in many memories. Fortunately, these temporary discomforts subside, usually leaving no physical scars. However, we are presently confronted with considerations of a disquieting nature. Chronic exposure to sunlight has been cited, in a report by the Committee on Cosmetics of the American Medical Association, as a major influence in the development of cutaneous cancer and precancerous conditions.

In another report, Howell<sup>2</sup> offered clinical evidence to support the contention that there is a solar derivation for cutaneous cancer, while he also discussed the probable effect of sunlight in forcing premature "aging" of the skin, citing the fact that eventual degeneration of collagen was noted. Further evidence of cumulative injury due to irradiation from ultraviolet light, and of resultant skin "aging," was given by Cockerell,<sup>3</sup> who conducted a study of skin specimens sectioned from portions of the anatomy of people in various age groups. Knox,<sup>4</sup> also, indicts solar radiation as a cause of skin aging, and recommends more protection from it.

In addition abnormal sensitivity to ultraviolet radiation occurs in certain persons. Among them are patients with lupus erythematosus, solar herpes, polymorphous light eruptions, keratoses, skin cancer, or photosensitivities induced by drugs, and patients who have had radiation therapy. The most common is the type of skin that freckles.

In the wake of this rapid accumulation of data, we are left with the obvious task of determining preventive measures. In some other areas of common human habit, where deleterious consequences are involved, cessation of non-essential pursuits can be recommended, but certainly the case against

<sup>\*</sup>Dr. Finnerty was assisted by Hollis Garrard, M.D., Miami, and by Richard K. Brown, M.D., Boston.

sunshine cannot so easily be closed. People cannot hibernate under shade, nor should they be encouraged to curtail outdoor activity due to fear of the sun.

#### Erythemal and Tanning Mechanisms

The principal effects of sunlight on human skin are conveyed by ultraviolet wavelengths shorter than 3200 ANGSTROM units. Although these constitute but a tiny fraction of total solar energy, approximately 0.01 per cent, they produce the various responses of sunburn, tanning, antirachitic action, and cutaneous cancer.<sup>5</sup>

The phenomenon of tanning is explained by the production and migration of melanin, actuated when skin absorbs ultraviolet energy contained in the wavelengths between 2900 and 3200 ANG-STROMS. This radiation stimulates the production of new melanin granules in melanocytes of the basal layer of the epidermis and the outward migration of pigmented cells and granules. Thickening of the stratum corneum, important in sunburn protection, is also induced.

Pigment migration does not begin until at least 24 hours after exposure, and new pigment formation requires several days. The quantity of melanin synthesized is directly related to absorption of energy, but a limit is reached beyond which continued insolation will not result in a significant increase in melanin production. For any one exposure period, therefore, there is a limit to the degree of tan development.

The same wavelengths that cause tanning are responsible for erythemal and painful sunburn reactions, but the erythema itself is not believed to be functional in the tanning mechanism. It is merely a concomitant result of ultraviolet irradiation, and therefore its degree of coloration acts only as a measure of the amount of energy which has been absorbed. Ultraviolet induced erythema does not necessarily entail pain, and the degree of redness is not a reliable indication of expected discomfort when applying to different individuals. Differences in coloration are meaningful only when related to each other on a particular person, in which case they can be a guide to the length of exposure required to produce pain.

Radiation of ultraviolet wavelengths above 3200

ANGSTROMS will also produce some pigmentation, since the absorbed energy will cause oxidation of existing pale melanin. The pigmentation induced is yellowish rather than brown. This oxidative darkening is the only type of quasitan that can occur relatively quickly, as over a weekend. However, it does not involve formation of new melanin granules, migration of particles, or thickening of the stratum corneum, and it does not afford significant protection from future erythemogenic exposure.

#### Protection From Solar Radiation

The role of the physician in giving counsel about solar exposure raises the question of what assurances may be given regarding development of a pleasing tan without severe sunburn. Healthful outdoor activities and tanning are so widely accepted as desirable that the reliability of measures commonly used to promote tanning and prevent sunburn requires evaluation.

The immediate discomforts of sunburn can be avoided by arranging gradual exposure to sunlight over a period of time. An exposure of perhaps 15 to 20 minutes on the first day, followed by regularly increasing exposure periods of consecutive days, will eventually promote a building-up of natural immunity to ultraviolet induced painful erythema. The immunity is apparently a result of at least two important physiological reactions to energy in the region of 2900 to 3200 ANGSTROM units.

The first of these is the synthesis of new melanin granules in the melanocytes of the basal layer. The granules then begin a migration upward, producing the tan pigmentation, which acts as an ultraviolet filter. The second change occurs in the stratum corneum, which becomes thickened and offers protection against further erythmogenic irradiation. Therefore, by gradual and controlled exposure, sufficient shielding against painful erythema may be gained in a great number of persons. However, so rigorous a scheduling of activity is not feasible for the average person. Further, the dangers inherent in excessive insolation continue, regardless of the method used to develop erythemal immunity.

The hazard of sunburn most often involves per-

sons who begin a vacation with untanned skin or who wish to spend a day out-of-doors in bright sunlight. Such persons must either limit the duration of exposure, or wear protective clothing, or use a sunscreen preparation that permits relatively long exposure without the penalty of a painful or serious burn.

Preparations containing chemical filters for ultraviolet light below 3200 ANGSTROMS are available that promise an acceptable procedure for the prevention of sunburn and, by interception of ultraviolet radiation before it reaches the skin, have the potential of becoming a primary preventive measure against the extremely deleterious long-range effects of exposure to sunlight.

#### Present Study

Although there have been a number of reports on the consequences of exposure to continuous, direct, and intense ultraviolet radiation, there is a need for more information on the effectiveness of sunscreen preparations under typical environmental conditions.

#### Materials and Methods

#### General Considerations

The present study was designed to investigate the effects of solar ultraviolet radiation under actual seaside conditions and to test the efficiency of a sunscreening agent as a method of protection against ultraviolet rays. Under conditions of actual human exposure, the quantity of ultraviolet radiation striking an individual is tempered by a variety of environmental considerations. The time of year, hour of day, weather conditions, and location are all of importance.

The time of year and hour of day reflect the situation of the sun with respect to the earth, determining the angle at which solar radiation strikes. Radiation is most intense on the first day of summer. In the northern and mid-northern sections of the United States, ultraviolet radiation is at its peak during the months of May through August. As the geographical position moves southward toward the equator, the intensity of ultraviolet radiation increases to become a danger throughout the entire year.

Assuming a month and location consistent with sunburn danger, the time of day must then be considered. At noon the sun is directly overhead and therefore presents the most potent radiation of the day. The angles of the sun's rays striking the earth before 8:00 A.M. and after 4:00 P.M. are so oblique as to reduce erythema-producing energy to an inconsequential amount. Truly threatening radiation is further limited to the period from 10:00 A.M. to 2:00 P.M., on a standard time basis.

Considerations of weather are obvious. Particular caution should be observed on a day that is hazy but not heavily overcast. Under conditions of haze, which scatters radiation, the threat of severe burn is sometimes underestimated.

The particular location where exposure occurs is another factor that is often neglected, because people are not generally aware that the effects of solar energy are multiplied by reflections from sand and water. When the influence of location is considered, the type of activity normally associated with a particular site should be included.

#### Selection of Test Preparations

Since the study was to be basically of a practical nature, it was decided to use a sunscreening preparation commonly available. A sunscreening preparation\* that appeared to possess the requisite attributes to be effective under beach conditions was selected.

To provide an experimental control, some test areas were to be exposed to sunlight without the protection of any agent. As an additional control, baby oil was chosen. Many people erroneously consider baby oil, along with mineral oil and vinegar, to be efficacious in providing protection against ultraviolet radiation.

A special problem involved in the mechanics of testing was how to provide complete protection for all exposed portions of the body not under test control. For this purpose a special sunstopping preparation† was used. It was found, in preliminary tests, to act almost as a shutter against radiation between 2900 and 3200 ANGSTROMS.

#### Test Locations and Weather Conditions

The tests were conducted at two beach sites. Test locations below 30° N. (Miami, Florida) and above 40° N. (Plymouth, Massachusetts) were

<sup>\*</sup> Bronztan Cream (Shulton) † Sun/Stop (Shulton)

selected, to evaluate subjects at two different geographical locations.

Exposure of the subjects for testing took place between 10:00 A.M. and 2:00 P.M. Eastern Standard Time, when ultraviolet radiation is the most intense. The weather at both test locations afforded intense sunslight, as is attested by the United States Weather Bureau data in Table 1.

Table 1 United States Weather Bureau Data

M	iami, Florida - March 19, 1961
Temperature	High, 82°; Low, 73°
Cloud Cover	Partly cloudy; 11 hours and 8 minutes of sunshine; 92% of possible sunshine
Wind	From the southeast, 9.8 miles per hour
Humidity	76% at 7:00 A.M., 73% at 7:00 P.M.
Plymo	outh. Massachusetts — July 22, 1961
Temperature	High, 86°; Low, 68°
Cloud Cover	High cloudiness on 9/10th of the sky cover, middle clouds occasionally; 11 hours and 10 minutes of sunshine; 76% of possible sunshine
Wind	From the west-northwest, 8.3 miles per hour
Humidity	High, 84%, 6:00 A.M., Low, 49%, Noon

#### Natural Exposure and Activities During Tests

The test subjects were specifically instructed to engage in normal beach activities during the testing periods, with the exception of swimming. Since they conducted themselves normally, under natural environmental conditions, the subjects did not receive unremitting direct exposure to ultraviolet radiation during the entire testing periods, and their test reactions could be interpreted as being directly applicable to the average person's experience during a beach outing.

The use of beach sites for the tests insured the influence of such important environmental variants affecting erythemic reactions as haze dispersion, wind, humidity, salt spray, and reflection from sand and water. Testing with artificial ultraviolet irradiation would not have given data as relevant to natural conditions of exposure to sunlight.

#### Subjects

A sufficiently large number of subjects was used to insure the inclusion of various ages and a diversity of skin types (Table 2). The recruitment of volunteers to participate in the tests posed some

Table 2

Data on the 169 Subjects Who Completed the Tests

Test Location	n	No. Subj		Sex	No. of Subjects
Florida		56		Male	75
Massachusett	ts	113		Female	94
		169			169
Complexion Type	No. of Subjects	Hair Color	No. of Subjects	Age	No. of Subjects
		Red	10	Under 21	79
Fair	90	Blonde	54	21-35	43
Medium	65	Brunette	88	36-50	40
Olive	14	Black	17	Over 50	7
	<b>—</b> →				
	169		169		169

difficulties, for although the test requirements allowed normal activities at the beach sites except for swimming, the subjects had to return 24 hours and six or seven days later for re-examination. Potential subjects were examined to insure lack of previous tanning. Of the 264 persons who started the tests, 169 completed them.

A special group of test participants comprised eight small children. While their families took part in the complete testing procedures, the sunstopping preparation was applied to these children, to protect their entire bodies from exposure.

#### Application of Test Preparations and Timing

The test preparations were applied and the exposures were timed under the supervision of the investigators. A staff of nurses carried out the necessary procedures.

The backs of the subjects were used for the areas of controlled isolation because this portion of the anatomy is relatively flat and uniform and is exposed during normal beach activities. A special die-cut tape was used to outline three rows, with three squares of skin exposed in each row, so that rigid control of irradiation could be maintained. Each of the nine squares provided four square inches of test area.

The first row of three squares was exposed with no protective agents applied, and this section constituted the experimental control. Across the second row 0.5 cubic centimeters of baby oil was spread before exposure to act as a blank. The third row was used as the experimentally protected area. To this area 0.5 cubic centimeters of the sunscreen

preparation was applied. The specified quantities of 0.5 cubic centimeters (0.45 to 0.55 cc's) were used to provide a layer of material over the test areas of approximately 0.04 millimeters thickness, which is the approximate amount of protective agent (suntan preparation) normally applied in average usage.

Exposure of the test areas to the sun took place between 10:00 A.M. and 2:00 P.M. Eastern Standard Time, when ultraviolet radiation is most intense. Unprotected skin cannot be exposed for four hours without risk of serious burning, and the nine test areas afforded a means of regulating individual dosages of sunlight.

To minimize the possibility of discomfort due to excessive sunburn pain, the first two rows were exposed only up to two of the four hours during the test. The middle two hours, 11:00 A.M. to 1:00 P.M., were used for exposure of these rows to insure maximum possible solar intensity. The third row received up to the full four hour exposure as it was anticipated that this row would have protection.

The squares provided a means for irradiating portions of each row for varying time periods, so that in the first two rows, squares Number 1 had exposure of 30 minutes each, squares Number 2 were exposed for an hour, and the Number 3 squares received the full two hour exposure. The three squares in the sunscreen protected row were exposed for two, three, and four hours, respectively. A masking tape was used to cover the squares until exposure was to begin and to cover them again after each time limit. All tapes were removed at the conclusion of the test.

All of the subjects were given the special sunstopping preparation and instructed to apply it to all exposed parts of the body except the taped test area. In addition, the eight small children used the sunstopping preparation.

#### Evaluation of Test Reactions

A standardized method of evaluating the test reactions was developed, as follows:

Twenty-four hours after exposure the subjects' backs were examined for erythemal reactions. A standard erythemal grading key was used (Table 3).

Table 3 Erythemal and Tanning Grading Keys

Erythemal Grading Key	Tanning Grading Key
0 No erythema	0 No tan
x. Minimum per- ceptible erythema	x Minimum per- ceptible tan
xx Definite erythema	xxDefinite tan
xxx Vivid erythema	xxx Dark tan
xxxx Vivid erythema w/pain	
xxxxx Blistering burn	

Each square was graded according to its degree of erythema in relation to the other squares. This method minimized the subjective element introduced by visual measurement. At the same time, color photographs were taken of the subjects' backs.

Six or seven days after exposure, when pigment formation and migration had had time to occur, the subjects were re-examined to evaluate and record the degree of tanning which had developed. A similar visual method of evaluation was utilized, with a standard key for tanning (Table 3). A second set of color photographs was taken.

A case record of each subject was kept, with observations entered by one of the investigators after each examination.

#### Results

The results of exposure to sunlight for up to four hours were tabulated according to the standard grading keys for erythema and tanning used by the investigators.

#### Erythemal Reactions

The erythemal reactions to two hours exposure, as evaluated on examination 24 hours later, are shown in Table 4.

Table 4
Degree of Erythema from 2 Hours of Exposure,
Expressed in Percent of Subjects

		Subjects' Test A	rea
	Unprotected	Baby Oil	Sunscreen
Grade of Erythen	na		
0	0.6	0.0	20.7
x	10.0	9.5	62.7
XX	29.6	32.0	13.6
xxx	51.5	53.3	3.0
or more	8.3	5.2	0.0

The differences in erythemal reaction between unprotected skin areas and areas coated with baby oil are not statistically significant. It was concluded that baby oil affords no protection against solar radiation. Of the unprotected areas and the baby oil coated test areas, 90 per cent developed Grade xx, xxx, or xxxx erythema (definite, vivid, or vivid with pain). Fifty-nine per cent developed Grade xxx or xxxx erythema.

In contrast, only 17 per cent of the sunscreen protected areas developed Grade xx to xxx erythema. Three per cent developed Grade xxx, and none developed a higher grade. The effectiveness of the sunscreen preparation was clearly demonstrated.

A minimum perceptible erythema (Grade x) was acquired by 63 per cent of the sunscreen protected test areas.

The unprotected areas and the areas coated with baby oil were not exposed for longer than two hours because of the likelihood of severe sunburn. Two hours of exposure produced Grade xxx or xxxx erythema (vivid or vivid with pain) in more than half of the subjects. Exposure to intense sunlight for two hours entails definite damage to the skin unless some effective protective measure is employed.

Areas protected by the sunscreen preparation were exposed for four hours. The results are shown in Table 5.

Table 5

Degree of Erythema from 4 Hours of Exposure, Expressed in Percent of Subjects

	Sunscreen Test Area
Grade of Erythema	
0	6.5
x	19.5
xx	49.7
xxx	23.7
XXXX	0.6
or more	

With the sunscreen protection, test areas exposed for four hours developed Grade x erythema (minimum perceptible) in 20 per cent of the subjects, Grade xx (definite) in 50 per cent, Grade xxx (vivid) in 24 per cent, and Grade xxxx or more (vivid with pain) in less than one per cent. This latter figure must be ascribed to experimental error and is not statistically significant.

Chart 1 illustrates the relationship of the time of exposure to the degree of erythema for the subjects as a whole. With two hours of exposure, the sunscreen protected test areas developed Grade x (minimum perceptible) erythema rather than the greater than Grade xx (definite) erythema of the unprotected and baby oil coated areas. Even with four hours of exposure, sunscreen protected areas, statistically speaking, developed less than Grade xx (definite) erythema.

It should be noted that the times specified in these results do not represent periods of direct and continuous exposure. Since normal activity was permitted, the subjects moved about and left the beach for short periods, reducing the actual times of exposure up to 20 minutes. This time factor is of minor importance in interpreting the reactions of the protected areas, as is evidenced by the relatively slow-moving erythemal progression for sunscreen protected areas shown in Table 4.

However, longer exposure undoubtedly would have increased erythmogenic reactions and pain significantly for the unprotected and the baby oil coated areas. With the timing element considered, those areas were actually exposed for less than two hours. Studies by Luckiesh<sup>6</sup> have shown that 50 minutes of exposure to sunlight will result in vivid erythema and 100 minutes in painful sunburn.

#### Tanning Reactions

The degree of tanning was evaluated six or seven days after exposure, because the formation of new melanin granules and their upward migration takes several days to become evident.

From two hours of exposure, Grade xxx (dark) tan developed in 20 per cent of the subjects' unprotected test areas, in 33 per cent of the baby oil coated areas, and in five per cent of the sunscreen coated areas (Table 6).

Table 6

Degree of Tanning from 2 Hours of Exposure,
Expressed in Percent of Subjects

	Unprotected	Baby Oil	Sunscreen
Grade of Tanning			
0	4.7	2.4	11.8
x	21.3	13.6	50.0
XX	54.0	51.0	33.0
xxx	20.0	33.0	5.2

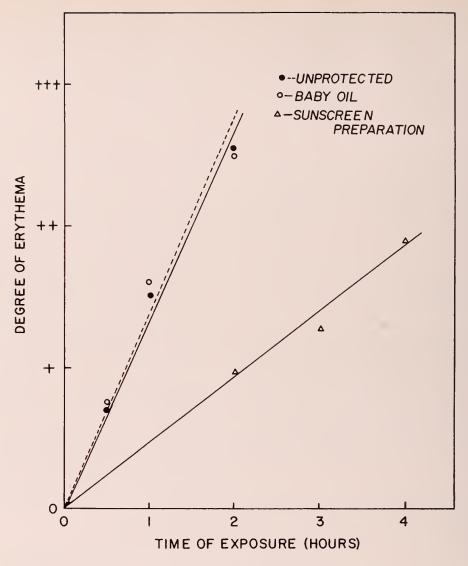


Chart No. 1

Four hours of exposure resulted in Grade xxx [dark] tan in 45.5 per cent of the sunscreen coated areas and in Grade xx (definite) tan in 40.3 per cent (Table 7).

Table 7

Degree of Tanning from 4 Hours of Exposure, Expressed in Percent of Subjects

	Sunscreen Test Area
Grade of Tanning	
0	1.8
X	12.4
XX	40.3
XXX	45.5

The average tanning reactions of the subjects as a whole are shown in Table 8. The sunscreen protected areas developed Grade xx (definite) tan from three or four hours of exposure, while the unprotected and the baby oil coated areas developed Grade xx from two hours of exposure.

The unprotected areas and the baby oil coated areas were not exposed for longer than two hours because of the likelihood that severe sunburn would result.

Table 8
Average Tanning Reactions

	Duration of Exposure				
	½ hour	1 hour	2 hours	3 hours	4 hours
Grade of Tana Developed	ning				
Unprotected	x	X	XX		
Baby Oil	x	x	XX		
Sunscreen			X	XX	XX

Enough short ultraviolet radiation to induce some degree of erythema is essential to activate the tanning process. The sunscreen protected areas afforded sufficient protection to allow exposure of four hours duration without the risk of severe sunburn and at the same time admitted enough ultraviolet radiation to cause the development of a definite tan.

The tanning reactions of the subjects reinforced present beliefs<sup>7</sup> that the degree of pigmentation is directly related to the degree of erythema developed, up to a limiting point. Erythemal reaction beyond an average grade of 2.5 will not increase the tanning significantly.

#### Sunstop Protection

If tanning is not desired, but continued exposure to sunlight is either wanted or unavoidable, a sunstopping preparation must be used. The sunstopping preparation used in the present study proved to be highly effective. Eight small children used it on all exposed skin areas. The other test subjects were instructed to apply it to all exposed parts of the body except the taped-off test area.

Where they failed to apply it uniformly, as on hard-to-reach areas, vivid erythema developed. When properly applied, the sunstopping preparation was found to block ultraviolet radiation shorter than 3200 ANGSTROMS, thus precluding both erythemic and tanning reactions.

#### Summary and Conclusions

The present study was undertaken to investigate the effects of exposure to solar ultraviolet radiation and to evaluate the effectiveness of a chemical sunscreen preparation under natural environmental conditions.

One hundred and sixty-nine subjects participated in the entire test and underwent ultraviolet radiation exposure for periods up to four hours while engaging in normal activities at seaside locations.

The erythemal reactions of skin-test areas (unprotected, coated with baby oil, or protected with a sunscreen preparation), were evaluated after 24 hours. These areas were re-examined six and seven days later when the formation of new melanin granules and their upward migration had had time to become apparent. The results were tabulated and compared.

The study confirms that exposure of untanned skin to intense sunlight must be restricted to brief periods until a protective tan develops. Otherwise, the average individual must apply a sunscreening agent that permits relatively long periods of solar exposure.

The preparation used in the test was found to admit sufficient radiation to activate the tanning process. The preparation absorbs sufficient ultraviolet radiation to prevent vivid erythema with pain.

The commonly applied preparation, baby oil, was found to afford no protection. The baby oil and the unprotected areas were exposed for periods no longer than two hours as a precaution against severe sunburn. The areas protected by the sunscreen preparation were exposed for periods up to four hours. Vivid erythema with pain occurred in less than one per cent of the subjects protected by the sunscreen preparation, a factor which must be ascribed to experimental error.

It was found that the preparation provided adequate protection for subjects with untanned skin to remain exposed to intense sunlight for periods up to four hours.

A definite tan was noted six or seven days following the suntest in the sunscreen protected areas. These areas had been exposed for periods up to four hours,

Among the unprotected areas, and the squares covered with baby oil, the same degree of tan was produced in two hours.

The test areas coated with baby oil developed definite erythema, vivid erythema, or vivid erythema with pain in 90 per cent of subjects after two hours of exposure.

These findings paralleled those of the unprotected areas. It was determined that baby oil affords no more protection against ultraviolet radiation than a complete absence of preparation.

The sunstopping preparation applied to all subjects, including eight small children, proved highly effective in blocking ultraviolet radiation, thereby preventing both erythemal and tanning reactions. The use of a complete sunstopping agent of this

type is a practical and effective method of preventing dermatological damage and resulting side effects. It may well be recommended to patients having conditions associated with photosensitivities or to persons unavoidably exposed to continuous insolation.

510 Commonwealth Ave.

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#### Writing Awards Judges Announced

Dr. Richard H. Orr, President of the American Medical Writers' Association, has announced that the Educational Committee of the AMWA will judge Southwestern Medicine's best article contest.

Contest rules are as follows:

Original scientific articles published in Southwestern Medicine will be eligible.

The contest for 1962 will close on Sept. 1, 1962, following publication of the August issue. Articles to be considered for publication in the August issue must be received by July 1, 1962. Articles not published with or before the August issue may still be eligible for publication and subsequent judging in the 1962-1963 contest running from Sept. 1, 1962 to Sept. 1, 1963. Only papers acceptable to the board of editors of Southwestern Medicine will be published.

Awards will be made in two classifications: Regional and National. All physicians who practice in West Texas, Arizona, New Mexico, Nevada, or Northern Mexico (States of Sonora and Chihuahua) will be eligible to compete for the regional awards. All physicians in the United States outside the regional area may compete for the national awards.

Awards will be made in the following amounts:

Regional: \$100 for the best paper, \$75 for the second best paper, and \$50 for the third best paper.

National: \$100 for the best paper, \$75 for the second best paper, and \$50 for the third best paper.

Contributions must be written in English, typed, double spaced on one side of paper only. A stamped, self-addressed envelope must accompany each paper to insure return of rejected manuscripts.

Papers should be submitted to Lester C. Feener, M.D., Editor, 310 North Stanton Street, El Paso, Texas.

#### The Medical Journal and its Advertising Pages

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Most medical journals as we know them today are a triangular composite formed by the journal itself at the apex and the readers and advertisers at the angles at the base. Each is dependent on the other, and each is of equal importance.

If the quality of the material published is not such as to attract and hold its readers then the journal has failed in its principal function. A journal which is the scientific publication of an organization and provides a service for its members has a particular obligation to furnish high quality. Everything starts from here.

Production costs being at an all-time high, subsidy by membership generally is insufficient, and outside income is required. This income comes from the advertisers, largely of the pharmaceutical industry. There is no compulsion on them to use the journal. It is purely a business proposition

which serves the function of calling attention to a drug about which the doctor has already been informed. We believe it is to the further advantage of the industry to keep worth-while medical journals going for the publication of unprejudiced descriptions of new, effective drugs and their clinical trials. Where else can this be done?

During the past year and a half the pharmaceutical industry has been reassessing its advertising policy. Also new government regulations on testing have slowed down the flow of new drugs to the market, with a consequent slowing of new drug advertising. As a result there has been a cutback in medical journal advertising ranging from 10 to 30 per cent over this period. All the medical journals have felt this and can but hope that any new policy which may be adopted will give due weight to the value of advertising in their pages.

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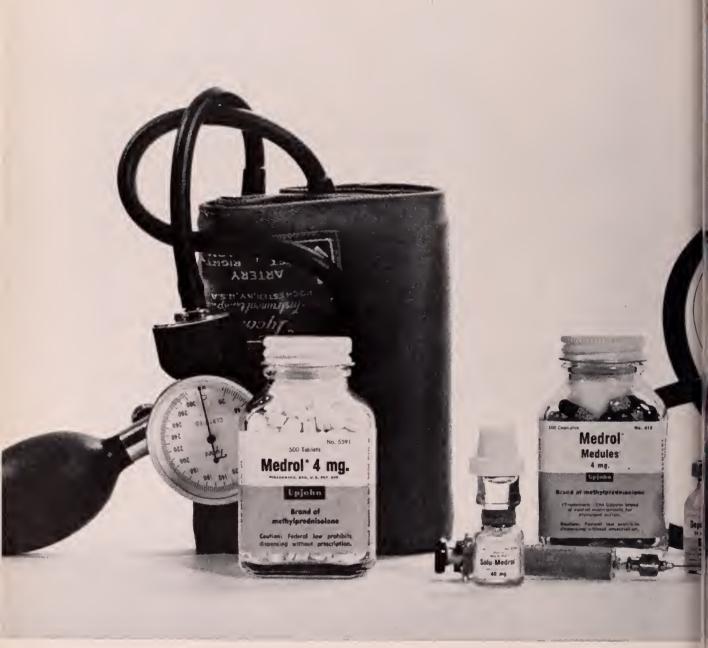
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1. Hodges, F. T.: *GP* 14:86, Nov., 1956. 2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

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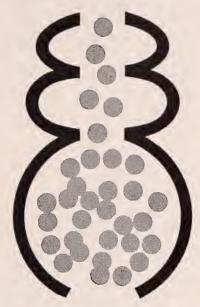
The usual dosage for infants and for children under twenty-five pounds is 5 mg. per pound every six hours; for children twenty-five to fifty pounds, 125 mg. every six hours. For adults and for children over fifty pounds, the usual dosage is 250 mg. every six hours. In more severe or deep-seated

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NOTE: Lomotil is an exempt narcotic preparation.

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- 1. Demeulenaere, L.: Action du R 1132 sur le transit gastraintestinal, Acta Gostraent, Belg. 21.674-680 (Sept.-Oct.) 1958.
- Kosich, A. M.: Treatment of Diarrhea in Irritable Colon, Including Preliminary Observations with a New Antidiarrheal Agent, Diphenaxylate Hydrochloride (Lomotil), Amer. J. Gastroent. 35:46:49 (Jan.) 1961.
- Weingarten, B.: Weiss, J., and Simon, M.: A Clinical Evaluation of a New Antidiarrheal Agent, Amer. J. Gostraent. 35:628-633 (June) 1961.

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VOL. 43

APRIL, 1962

NO. 4

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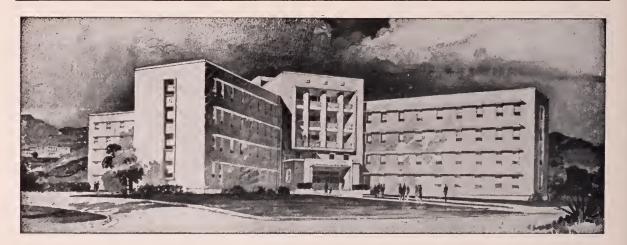
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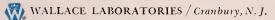


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#### Coming Meetings

Arizona Medical Association, Annual Meeting, Scottsdale, April 24-28, 1962.

New Mexico Medical Society, annual meeting, Hobbs High School, Hobbs, N. M., May 8-11, 1962.

Texas Medical Association, Annual Meeting, Austin, May 12-15, 1962. C. Lincoln Williston, 1801 North Lamar Blvd., Executive Secretary.

New Mexico Chapter, American Academy of General Practice, Summer Clinic, Ruidoso, N.M., July 16-19, 1962.

The Western Association of Railway Surgeons, annual meeting, Stockmen's Motor Hotel, Elko, Nev., Sept. 27-29, 1962.

Southwest Obstetrical and Gynecological Society, 12th Annual Meeting, Camelback Inn, Phoenix, Oct. 10-13, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.

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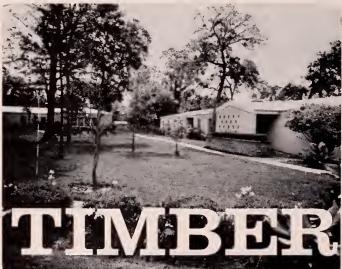
about dosage, possible side effects and contraindications.

References: 1. DeNyse, D. L.: M. Times 87:1512 (Nov.) 1959.
2. Gruenberg, F.: Current Therap. Res. 2:1 (Jan.) 1960.

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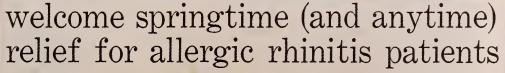
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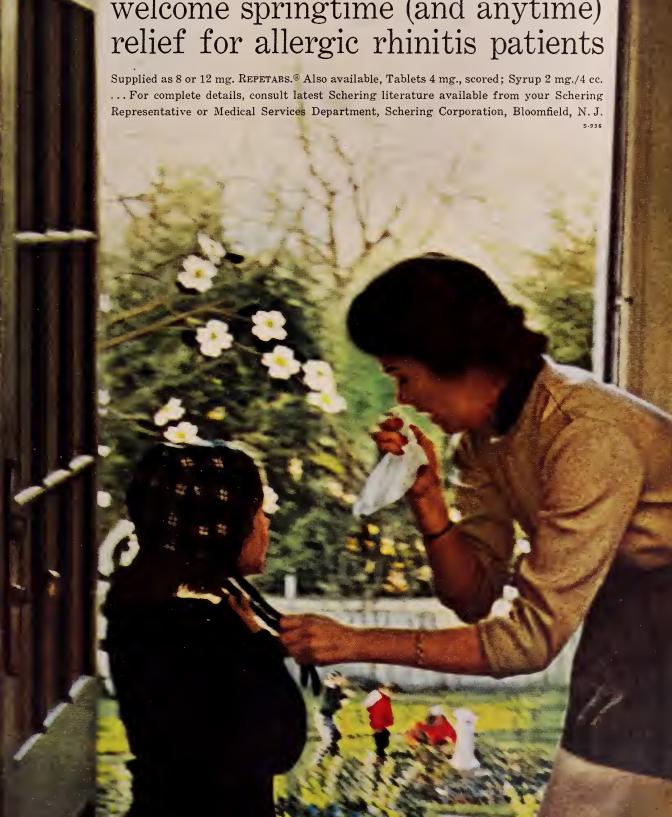
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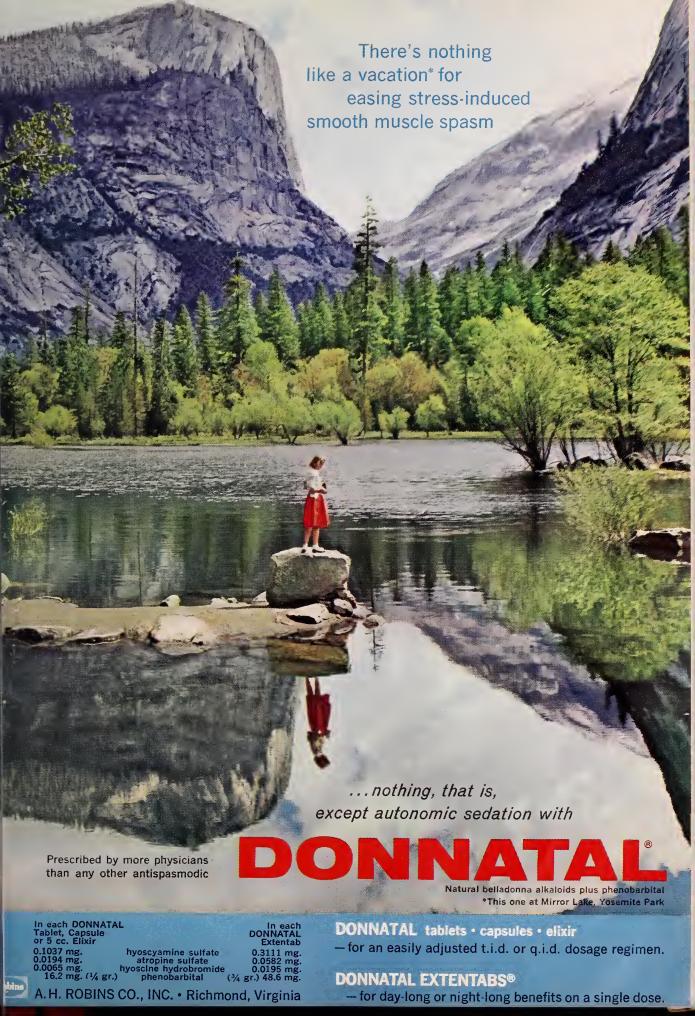
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References: 1. Carpenter, E. B.: South. M. J. 51:627, 1958. 2. Hudgins, A. P.: Clin. Med. 8:243, 1961. 3. Lamphier, T. A.: J. Abdomin. Surg. 3:55, 1961. 4. Levine, I. M.: Med. Clin. N. America 45:1017, 1961. 5. Meyers, G. B., and Urbach, J. R.: Penna. M. J. 64:876, 1961. 6. Perchuk, E., Weinreb, M., and Aksu, A.: Angiology 12:102, 1961. 7. Poppen, J. L., and Flanagan, M. E.: J.A.M.A. 171:298, 1959. 8. Schaubel, H. J.: Orthopedics 1:274, 1959. 9. Steigmann, F.: Am. J. Nursing 61:49, 1961.

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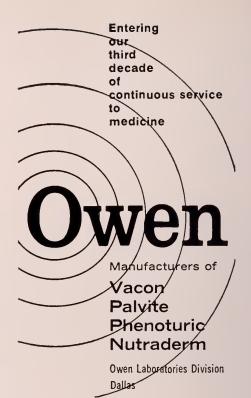
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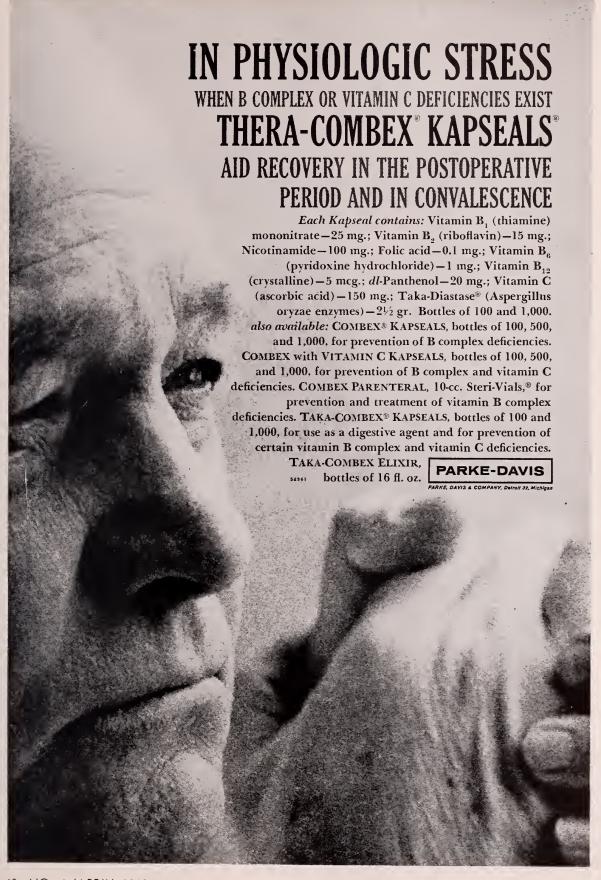
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# New Mexico Medical Society To Meet May 8-11 in Hobbs

The 80th annual meeting of the New Mexico Medical Society will be held in Hobbs, N. M., May 8-11, 1962.

Dr. George M. Fister, Ogden, Utalı, President-Elect of the American Medical Association, will speak on "Governments Can't Doctor" at a meeting open to the public at 8 p.m. May 9 in the Hobbs High School auditorium.

On the agenda with Dr. Fister is Dr. Vincent P. Collins, Houston, Professor and Chairman of the Department of Radiology of the Baylor University College of Medicine, who will talk on "When Cancer Happens".

Other speakers on the program will be:

Dr. George L. Jordan, Jr., Houston, Associate Professor of Surgery at Baylor University.

Dr. Richard H. Eppright, Houston, Assistant Professor of Orthopaedic Surgery at Baylor University.

Dr. Homer F. Weir, Houston, Assistant Professor of Pediatrics at Baylor University.

Dr. Marc Moldawer, Houston, Assistant Professor of Medicine; Chief, Endocrine Section, Baylor University.

Dr. Herbert Harris, Houston, Baylor University.



Dr. Fister

Dr. Reginald H. Fitz, Albuquerque, Dean of the University of New Mexico Medical School.

Officers of the Society are Dr. William E. Badger, Hobbs, President; Dr. R. C. Derbyshire, Santa Fe, President-Elect; Dr. C. Pardue Bunch, Artesia, Vice-President; and Dr. Hugh B. Woodward, Albuquerque, Secretary-Treasurer.

The complete program follows:

Monday, May 7

3:00 pm Council Meeting 6:30 pm Council Dinner

Tuesday, May 8

3:30 pm First Session of House of Delegates
High School Library
Reference Committee Meetings



Dr. Collins



Dr. Eppright



Dr. Jordan

Wednesday, May 9

8:00 am Registration

Theater Building

10:00 am Second Session of House of Delegates High School Library

> General Meeting Little Theater

Presiding: Allan L. Haynes, M.D., Clovis, Immediate Past President, New Mexico Medical Society

1:30 pm Invocation

C. Pardue Bunch, M.D.

Welcome

Mrs. Andra A. Kemnitz Mayor, City of Hobbs

Welcome

Coy S. Stone, M.D., Hobbs, President, Lea County Medical Society.

1:45 pm Presidential Address
William E. Badger, M.D.

First Clinical Session Little Theater

Presiding: William E. Badger, M.D.

2:15-3:00 pm Surgical Management of Occlusive Diseases in the Aorta and Peripheral Arteries

Coorga L. Jordan Jr. M.D.

George L. Jordan, Jr., M.D.

3:00-3:45 p.m. Recent Advances in Immunization

Homer F. Weir, M.D.

3:45-4:05 pm Visit Exhibits

4:05-4:50 pm Management of the Lymphoma Patient Vincent P. Collins, M.D.

6:00 pm Convention Buffet (no host) Hobbs Country Club

8:00 pm Public Lectures

High School Auditorium

Presiding: William E. Badger, M.D.

When Cancer Happens
Vincent P. Collins, M.D.

Governments Can't Doctor George M. Fister, M.D.

Thursday, May 10

Second Clinical Session

Little Theater

Presiding: R. C. Derbyshire, M.D.

8:30 am Registration

9:00-9:45 am The Physician's Role as a Leader in the Care of the Retarded Child

Homer F. Weir, M.D.

9:45-10:05 am Visit Exhibits

10:05-11:45 am Panel Discussion

The Diagnosis and Treatment of Osteoporosis

Osteoporosis

Moderator: Andrew M. Babey, M.D., Las Cruces

Participants: Vincent P. Col-

lins, M.D.

Richard H. Eppright, M.D. Marc Moldawer, M.D.

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Dr. Moldawer

12:00-1:45 pm Medical and Surgical Luncheon High School Cafeteria Presiding: Jack C. Redman, M.D., Albuquerque

### Third Clinical Session

### Little Theater

Presiding: C. Pardue Bunch, M.D.

2:00-2:45 pm Current Status of Tissue Transplantation

George L. Jordan, Jr., M.D.

2:45-3:30 pm Differential Diagnosis and Treatment of Vertigo

Herbert Harris, M.D.

3:30-3:45 pm Visit Exhibits

3:45-5:00 pm Panel Discussion

Complications of Continuing and Discontinuing Corticoste-

roid Therapy

Moderator: Reginald H. Fitz.

M.D.

Participants: George L. Jordan, Jr., M.D.

Marc Moldawer, M.D. Homer F. Weir, M.D.

6:00 pm Cocktails

Hobbs Country Club



Dr. Weir

7:30 pm Dinner

Hobbs Country Club

Entertainment: Doraine and Ellis, presenting "A Costumed Cavalcade of Broadway's Greatest Musical Hits"

Friday, May 11

Fourth Clinical Session

Little Theater

Presiding: Coy S. Stone, M.D.

9:00-9:45 am Renal Tubular Disorders and Re-

nal Stones

Marc Moldawer, M.D.

9:45-10:30 am New Methods in the Manage-

ment of Scoliosis

Richard H. Eppright, M.D.

10:30-11:00 am Visit Exhibits

11:00-11:45 am Recent Advances in Medical

Education

Reginald H. Fitz, M.D.

11:45-12:30 pm The Selection of the Type of

Treatment for Carcinoma of

the Larynx

Herbert Harris, M.D.

Specialty Group Meetings

2:00-5:00 pm New Mexico Chapter, American College of Chest Physicians.

# ORIGINAL ARTICLES

### The Ocular Care of the Pre-School Child\*

MAX FINE, M.D.. San Francisco

A question asked most frequently of the ophthalmologist by new parents is "When should I have the baby's eyes examined?" Assuming that this question indicates that the parent has observed no obvious malformation or abnormality of the infant's eyes I reply that the eyes should be examined sometime within the first six months and, provided no defect is found, again between the age of three and four. There are definite reasons for choosing these times.

The first examination, before age six months, is a screening examination and may properly be made by the pediatrician or the family physician. The purpose of this examination is to discover any gross abnormalities or congenital defects. One should note the position of the eyelids, whether the eyes appear straight, whether there is any limitation of motility or nystagmus. One should observe the transparency and size of the cornea, the depth of the anterior chamber, the shape and reaction of the pupil.

The presence of a bright red reflex from the fundus on ophthalmoscopic examination verifies the transparency of the lens and vitreous. Ophthalmoscopy should be performed with the pupil dilated while the infant is feeding. Mydriasis can be obtained rapidly in infants with a drop of two per cent homatropine or one per cent cyclogyl. The optic dise at this age is grayish pink in color, the margins are not sharply defined. Pigmentation of the retina is incomplete so that the fundus presents a pale tessellated appearance suggestive of albinism, particularly in the periphery. Visual

acuity at this age is of low order, possibly 20/200, and visual testing is limited to the child's ability to follow a small light or a small toy.

The diseases particularly to be looked for in this examination are congenital cataract, congenital glaucoma and retinoblastoma, which require immediate treatment. Strabismus which is present at this early age requires early treatment but is not in the same emergency category as the other conditions mentioned. These three conditions should be reviewed briefly.

### Congenital cataract

This refers to any opacity of the lens which is present at birth or develops shortly after birth. Etiologically, congenital cataract may be classified in three categories: 1) Hereditary cataract 2) Cataract due to metabolic disorders 3) Cataract due to infections during pregnancy.

Many morphologic types of congenital cataract have been described. Such a classification is useful clinically only insofar as it determines the degree of visual impairment. This impairment depends on the density, the size, and the location of the lens opacities. A small opacity situated in the anterior layers of the lens affects vision minimally. A similar opacity located at the posterior pole of the lens may interfere seriously with vision. Any degree of impairment up to perception of light may occur.

If the cataract is dense visual acuity does not develop normally due to the lack of a sharp retinal image. In such cases nystagmus will appear. Once such nystagmus is present it remains permanent, even though the cataract is removed. If the

<sup>\*</sup>Presented at the 431d annual meeting of the Southwestern Medical Association, Las Vegas, Nev., Oct. 21, 1961.

cataract appears some time after birth, when central visual acuity has developed nystagmus will not occur. When the cataract is unilateral and of sufficient density to reduce the acuity to a level of 20/50 or less, central vision does not develop normally and the eye will remain amblyopic even though the cataract may be removed. In such cases the amblyopic eye will often show a slight nystagmus of a vertical type.

Surgery in congenital cataract should be undertaken conservatively. It is to be considered only when visual acuity is reduced to a degree that the normal development and use of the eyes are not possible. In older children when visual acuity can be tested, experience has shown that this means an acuity of less than 20/50. If the acuity is 20/50 or better, the patient with congenital cataract is best left alone, able to avail himself of the advantages of normal accommodation and a normal pupillary mechanism. The usual indications for surgery are:

- 1. Bilateral complete cataract present at birth or shortly thereafter.
- 2. Bilateral dense opacities which are not complete.
- 3. Bilateral central opacities in which useful vision is obtainable only when the pupils are dilated.

The age at which congenital cataract in these catagories should be operated has been debated frequently. On one side is the desirability of establishing a clear retinal image as early in life as possible. On the other, is the disadvantage of performing surgery on a small immature eye.

Most ophthalmic surgeons believe that early surgery is indicated on at least one eye when bilateral dense opacities are present. The plan generally accepted when bilateral cataract of a degree sufficient to interfere with foveal fixation is present, is to operate on one eye when the child is six months old, in the hope that nystagmus may be prevented. Operation on the second eye is postponed till the child is two to three years old.

The visual results after operation for congenital cataract do not approach those after adult cataract. Falls' statistics indicate that only 53 per cent had visual acuity of 20/100 or better and

nine per cent had 20/200. Seventeen per cent were essentially blind. The rest has a visual acuity of less than 20/200. In respect to near vision only 18 per cent were able to read type smaller than Jaeger 7. About 50 per cent of infants with congenital cataract present other ocular abnormalities such as strabismus, nystagmus, aniridia. choroidal and retinal defects, microphthalmos and partial dislocation of the lens. There are, of course, also other developmental defects in many of these children. The prognosis for normal use of the eyes is therefore not a good one in surgery of congenital cataract.

### Congenital glaucoma

Congenital glaucoma refers to cases of increased intraocular pressure due to faulty development of the aqueous outflow channels in the angle of the anterior chamber. This defect may be present at birth or may appear during the first three years of life. The distention of the eyeball resulting from the increased pressure, while the sclera is still thin and soft, have given the disease the terms "buphthalmos" and "hydrophthalmos". The condition is transmitted genetically as an autosomal recessive characteristic. About two thirds of the affected children are male and about two thirds are affected bilaterally.

The signs which should call attention to the possibility of this disease are the following:

- 1. Sensitivity to light.
- 2. Excessive tearing.
- 3. Rubbing of the eyes.
- 4. An abnormally large eye.
- 5. A corneal diameter greater than 12  $\mathrm{mm}.$
- 6. Cloudiness of the cornea.
- 7. Ruptures or folds in Descemet's membrane.
- 8. Decreased intraocular pressure on tactile examination.

A positive diagnosis can be made only after examination under anesthesia when the intraocular pressure may be measured with the tonometer and the anterior chamber may be examined with a gonioscopic contact lens and microscope. If the diagnosis is confirmed the proper treatment is immediate surgery.

This is the operation of goniotomy which consists of a simple knife incision into the angle of the anterior chamber where the canal of Schlemm

is located. It is usually performed at the time of the verifying examination under anesthesia to avoid a second anesthetic. Prompt treatment results in control of the glaucoma in over 75 per cent of cases. Failure to recognize the disease in its early stages may mean irreparable loss of vision or even blindness. About 10 per cent of children in schools for the blind were affected with congenital glaucoma.

### Retinoblastoma

When one observes a white reflex in the pupil on ophthalmoscopic examination of an infant the possible conditions which come to mind are complete congenital cataract, retrolental fibroplasia, and retinoblastoma. The possibility of cataract may soon be established or ruled out by dilating the pupil and examining the lens with oblique illumination.

Retrolental fibroplasia, now an extremely rare disease, may be ruled out in the absence of a history of prematurity and by examination of the peripheral fundus with the dilated pupil. It must be kept in mind that a few cases of R.L.F. have been reported in full term infants. There remains then the highly malignant tumor of the retina, retinoblastoma.

This tumor appears as one or more dense yellowish white masses in the retina, extending into the vitreous cavity. When sufficiently large the white mass may be observed through the pupil under ordinary illumination and frequently is noted by the parents. The tumor is always congenital but in some cases active growth is delayed until some time after birth. The average age at which the tumor is discovered is two years.

Fortunately the tumor is a rare one. It has been estimated that the yearly number of retino-blastoma cases in this country would be about 100. The tumor is bilateral in about one third of the cases. This bilaterality is not due to extension through the chiasm but is due to multiple sites of origin. In bilateral cases the tumor is usually less advanced in one eye than in the other, and the tumor in the second eye may not become apparent until some months or years after the first eye has been removed.

Spread of the tumor is both by extension through the optic nerve and much more rarely

through the sclera, as well as by metastasis through the blood. Retinoblastoma is a dominant trait, although sporadic cases are well known. On the basis of statistical studies the normal parents of a child with retinoblastoma have about one in one hundred chance of producing another child with retinoblastoma.

The patient himself, however, presents an entirely different problem if he survives the tumor. Each of his offspring will have a fifty per cent chance of retinoblastoma. On the basis of statistical studies this chance is even greater.

Treatment of retinoblastoma has progressed a great deal. In unilateral tumor the safest treatment is immediate enucleation. In bilateral tumors the plan commonly accepted is enucleation of the more severely affected eye and treatment of the fellow eye with irradiation and TEM unless it appears hopeless also. Reese has reported a five year cure rate of 75 per cent with this plan of treatment.

More recently there have been some encouraging reports of destruction of smaller tumors by photocoagulation. Most important is the frequent re-examination of the fellow eye for a period of at least two years after an apparently unilateral tumor has been removed.

The second eye examination, which I have suggested should be made between the age three and four, in addition to a careful examination of the ocular structures should include a measurement of the visual acuity, a study of the fusion mechanism and the ocular motility, and a refraction under cycloplegia when indicated. The defects with which this examination is particularly concerned are strabismus, high errors of refraction and amblyopia.

A screening type of examination may be made by the pediatrician or family physician. The average child at age three may be tested with the kindergarten chart. Many children at this age are sufficiently advanced to be tested with the more accurate E chart. By age four the average child can be tested with the E chart. The usual visual acuity at this age as tested on such charts is 20/30. If the visual acuity in each eye is 20/30 and there is no evidence of strabismus referral to an ophthalmologist is not necessary. How-

ever, if the visual acuity is less than 20/30 in one or both eyes, or if there is evidence of strabismus it is urgent that the child be seen by an ophthalmologist at this time.

The principal reason for prompt referral at this age is the possibility of amblyopia. This term in its strict sense means dullness of vision from any cause. In the sense in which it is used by the ophthalmologist it refers to faulty vision in one eye in the absense of any organic eye disease. About four per cent of young adults are so affected. The two principal causes of such amblyopia are strabismus which causes so-called amblyopia ex anopsia (amblyopia from disuse) and a marked irregularity in the refraction of the two eyes which produces amblyopia due to anisometropia. The mechanism in the two types of amblyopia is very similar, and often both factors operate.

The function of vision is not fully developed at birth but improves steadily up to about age seven. Thus we have said that at age one year the acuity is probably not much more than 20/200 and at age four about 20/30. If anything interferes with the constant use of one eye visual acuity becomes arrested at a low level and may remain so permanently.

The interfering factor may be strabismus. In this case the crossed eye has its fovea directed to a different object than the fixing eye. The result would be diplopia which is intolerable. The brain corrects this intolerable situation by suppressing the image of the crossed eye. Such a habitual suppression of foveal vision results in amblyopia.

This occurs regularly in children with monocular strabismus in which the same eye is crossed constantly. It does not occur in alternating strabismus in which the eyes are used alternately and equally but not binocularly. The visual suppression resulting in amblyopia ex anopsia has specific characteristics:

- 1. It is probably a functional defect of cone vision. The peripheral field is not impaired but only the central field in which there appears to be a scotoma.
- 2. The eye appears peripherally normal on ophthalmoscopy.
- 3. The use of the better eye tends to reinforce the amblyopia.

- 4. The degree of amblyopia (the level of visual acuity) remains constant through life unless it is treated
- 5. The child may develop an anomalous retinal correspondence.

This means that an attempt is made to combine the foveal vision of the better eye with a nonfoveal point in the retina of the crossed eye. This results in an incomplete or faulty type of fusion which makes treatment of the strabismus more difficult and reinforces the amblyopia.

The mechanism of amblyopia due to unequal refraction of the two eyes is similar. The infant and young child does not have sharp foveal vision and is more concerned with near regard than distant objects. It therefore favors the eye which is less far sighted or hypermetropic when the refraction of the two eyes is different. The difference between the two eyes is usually two diopters or more before this occurs. Thus the more far sighted eye will not receive a clear foveal image even though it is straight. The end result is the same as in monocular strabismus—a failure of visual development.

The treatment of amblyopia, if begun early, is simple and effective. It consists of occluding the sound eye to force the child to fixate the fovea of the amblyopic eye. The earlier this treatment is begun the shorter is the period required to bring the visual acuity to the level of the fellow eye. In the two year old child this may take a month. In a six year old child this will often take six months and in some the level of the other eye is never reached. After age of seven the chance of obtaining significant improvement of the amblyopic eye is very poor although in most instances a trial should be made.

The most important factor in the prevention of amblyopia is the examination of the eyes between age three and four. Newer technics of overcoming amblyopia have been introduced in the past few years which hold some promise of correcting amblyopia even in adults. The evidence to date, however, indicates that early recognition of amblyopia is still the most important step in its treatment.

#### Strabismus

The management of strabismus will be covered here very briefly, since I am informed that this subject was presented here about a year ago.

Intermittent convergent strabismus may be observed in infants and young children for some time before definitive treatment is necessary. This is true only if the deviation is occasional. Constant monocular strabismus requires prompt treatment to prevent amblyopia as well as to restore binocular vision. The strabismus which appears at birth or shortly thereafter often has an anatomic defect as its basis. The strabismus which appears after age two is most often accommodative—that is associated with a hypermetropia or hypermetropic astigmatism.

Patients with a constant alternating strabismus usually show the condition at birth or within the first few months. Since each eye is fixated, alternately, there is no problem of amblyopia. The problem here is one of trying to maintain binocular vision and of correcting a cosmetic defect. These patients should have surgical correction of the strabismus early in life, usually at age two. One may generalize that a strabismus which appears early—that is before age two or three should be operated early. Those appearing after age three, who have had a period of binocular vision, may more often be treated without surgery.

Divergent strabismus presents a different prob-

lem. Most of them are intermittent in nature. Some will show frequent or constant divergence when fixing in the distance and no strabismus at near fixation. Others may show the reverse.

The greatest number of patients with divergent intermittent strabismus are sometimes divergent for distance and sometimes slightly divergent for near. Often these are overlooked because the child shows the divergence only when fatigued or sleepy, and only when fixing in the distance. These children often tend to close the diverging eye in sunlight.

Since the divergent strabismus is intermittent and may not be present in near fixation, amblyopia does not develop and early treatment is not as important as in the convergent group. Surgical correction of the intermittent exotropia is very effective but may be postponed until the early teens and in cases in which it is of small degree and produces no symptoms may be postponed indefinitely.

A constant divergent strabismus, on the other hand should always be investigated immediately since it may be paralytic in origin and since amblyopia may occur.

655 Sutter St.

Cabeza de Vaca performed what probably was the first surgical operation by a white man within the present limits of the United States. This procedure was excising an arrow from an Indian's arm, and was done in the southeastern corner of New Mexico almost a hundred years before the Pilgrims landed.

A History of Abdominal Surgery
By Maxine O. Dellinger, Las Vegas, N. M.

### On The Nose

M. P. SPEARMAN, M.D., El Paso

In the year 6000 B.C. a papyrus describes the treatment of nasal fractures and the use of pressure dressings. Since then, for these thousands of years, heated argumentation and discussion among practitioners of the art of medicine has lighted the dark horizons of our limited knowledge even as distant lightning on a summer night. Out of the din of these voices of the centuries has come some truths, basic to the intelligent practice of rhinology. Many vehement pleaders and advocates have appeared on the scene, briefly but noisily, and have withdrawn into the shadows of the past. Woven into the cacophony is the eternally recurrent theme "don't monkey too much with nature's way." And that is a valid text for today, in all medicine.

Hippocrates (460-370 B.C.) stressed the importance of reducing nasal fractures within twenty-four to thirty-six hours. He devised a method of removing nasal polyps, using sponges. Claudius Galen (130-200 A.D.) recognized the nasal membranes as part of the air conditioning system for the lungs. Avicenna (980-1036) advocated ligatures for nasal polyps. Leonardo da Vinci (1452-1515 described the maxillary and frontal sinuses.

It was 1651 when Highmore described the maxillary sinus. Should not this then be called the "antrum of da Vinci?"

Fallopius (1523-1562) described a snare-like operation for nasal polyps. Aranzi (1530-1589) observed the interior of the nose by directing a beam of sunlight through a hole in a wooden shutter. Petrus Forestus (1522-1597) described ozena. Valsalva (1665-1723) described a method of forcing air into the middle ear space via the Eustachian tube. Niemann (1860) discovered the anesthetic properties of cocaine, destined to be of value in nasal surgery. Meyer of Copenhagen (1868) described the adenoid. Politzer (1870) said that "everything is connected with everything"—thus demonstrating an awareness of the whole patient.

Today we make much of psychosomatic medicine, and insist, as if it were a latter-day revelation, that the patient cannot be divided, like Gaul, into various parts; but must be viewed, understood and treated as a whole being. In 1875 Adams attempted surgery on the septum, followed in 1882 by Ingalls who performed the first submucous resection in the United States. Takamine (1901) discovered and developed the uses of epinephrine. Sometime later Barnes discovered and exploited a "silver proteinate" destined to occupy the throne room of nasal therapeusis for too many years.

During the 16th century great efforts were made by anatomists to assign functions to various structures. It was held that the sinuses filtered air before it was drawn into the brain, that they contained a mucous humor which moistened and lubricated the eyes and the nose. Some believed that the sinuses generated animal spirits, and that they drew in odors, releasing them to the brain. Schneider (1660) wrote the first description of the nasal mucosa. From that point of departure developed the modern knowledge of its structure and function.

### Plastic Surgery

It is of interest to note that, also in the 16th century, plastic surgery of the nose was condemned by the church as being the craft of the devil and interference in God's handiwork. So effective was this opposition that very little was accomplished in this field for nearly two hundred years. Because of the deep mystery of life and death, of structure and function, the advancement of man's knowledge, especially in the realm of medicine, has been hampered, hounded and hindered by superstition, misplaced theology, and physical and mental violence to the man of curiosity, who only sought to learn.

In the time of most of us now in the practice of rhinology certain fads have come and gone. not being based entirely on common sense; all presenting a distinct interference with normal tissue functions. Many held for years that submucous resection would cure deafness, and a heap of removed cartilage bore its mute testimony to the uselessness of that notion. Physiology text books, in use by the grammar and high schools of this country, depicted a child with an idiotic expression, labeled "the adenoid face". Slow learning, socially unacceptable toilet habits, tendencies toward criminality-much could be cured by removal of the adenoid! Unusual susceptibility to colds was supposed to be relieved by submucous resection, or by curettement of the ethinoid cells. Headache could be cured by letting air into the antra.

Sometimes patients are treated for vacuum headache from the frontal sinuses, when X-ray studies may reveal a complete absence of those sinuses! Gallons of the brownish, thick liquid, patentered as a "silver proteinate", have been stuffed into innocent noses, via the wad of cotton poked and shoved upward, hoping to cleanse and sterilize the sinuses. Long strings of brownish, glairy mucous oscillate and snap from the nasal orifice fol-

lowing the extraction of the mass of filthy cotton. This may impress the patient, but is worthless otherwise. Some people just cannot pass up any unplugged orifice.

Some rather questionable procedures are still in vogue today in some quarters. Not all useless notions have been quelled. The practice of removing the turbinates for what is really allergic hypertrophy does not reflect much credit upon the surgeon, nor does it alter the allergy of the patient. Many children are being subjected to adenoidectomy to provide adequate nasal ventilation, when the true diagnosis is allergic rhinitis. Two, three or even four such operations on one child would seem to partake of beautiful ignorance.

Sometimes, in our zeal to achieve complete verticality of the septum, we may overdo the sub-inucous resection, and end up with excessive hemorrhage, perforations and collapse of the entire nose. The objective of the operation is to secure adequate nasal ventilation only. To remove everything in sight is to paint the lily, after decent air space is achieved. Too much air space is most undesirable. There is no need to waste time in the removal of every tiny spur of the vomer. Sometimes the skill and competence of the surgeon is better exhibited by knowing when to stop, remove the gloves and depart from the operating suite. The watch-word in the entire field of rhinology should be simply this: do what is necessary and not harmful, and then stop.

### **Basic Nasal Functions**

Galen recognized that the nose was basically an organ of respiration. Steno (1662) knew about the true function of the mucous glands. Galen spoke of the functions of the turbinates in cleansing and warming the inspired air. Gray in 1928 wrote about the ciliated epithelium of the respiratory tract. From that time our understanding of the function of the nose has burgeoned.

Abundant and detailed studies on nasal physiology are available, but reducing this information to simplicity, one may say that the function of the nose is two-fold, viz., to breathe and to smell. Different types of mucosa are involved in these duties. Olfaction cannot, of course, proceed with

normality, unless the structure of the nose be somewhat near anatomically correct. For the functions of the nose depend to a great extent upon the contours of the nasal structure.

The mucosa must be accessible in proper proportions of exposure to the inspired air. That means that deformities tend to misdirect and alter air currents, that disease might impair the ability of the vessels and the glands of the mucosa to perform. Basically, then, as air is drawn into the nasal spaces through the nares it swirls over and around the turbinates. Because of the abundance of superficially placed blood vessels and mucous glands in this erectile tissue the air is warmed and moistened through the evaporation of the mucous.

To a fascinating degree, the turbinates may be thought of as being living baffle plates. Particles such as dirt, pollens, bacteria, etc., are trapped by the blanket of mucous present on the nasal mucosa. The trash is moved backward by the action of the cilia. It may then be sucked back and spat out, or if abundant, blown out by a forceful blast of expired air. Thus it is apparent that the nose is a marvelous air-conditioning apparatus. It can respond automatically to such modifiers as temperature, moisture, dust content, pollen concentration and noxious gases in the air. It follows then, that treatment of the nose should, above all, not create problems of iatrogenic nature.

Not medically, not surgically, has the physician the right to do anything to the nose excepting just enough to lend aid. He must learn that he cannot re-create this marvelous structure. It is incumbent that a basic understanding of what the nose is trying to do be possessed and used by the rhinologist. There is little sense in trying to sterilize the nose with drops or packs employing antibiotics or the sulfones. That is interference with the behavior of the nasal mucosa.

The only function of a nose drop is to shrink the mucosa, and to some slight extent, accomplish some mechanical washing and cleansing. For those reasons it should be mild in action, and quite dilute. Surgical procedures should be done very carefully, with minimum trauma, leaving normal tissue strictly inviolate. The supreme law is, to repeat, do only what is necessary, and then stop. Too many nasal cripples owe their creation to unwise surgical and medical interference with the physiology of the nose.

### Post-Nasal Drip

Rare is the rhinologist who has not witnessed the triumphant display of a carefully-wrapped, tenderly-hoarded exudative mass by its producer—the patient who has "suffered for years, Doc, from post-nasal drip." Learned lectures, and exhaustive treatises, have probed and explored into this problem. Now, it is well understood that sometimes the blood-streaked pile of trash in the nasopharynx is there because of disease, either in the nose, the sinuses or nasopharynx. After elimination of an actual disease process one must understand that the so-called "drip" may be just waste from the nasal air-conditioning function.

Its composition will be leukocytes, epithelial debris, dust particles, bacteria and pollens—in other words, partly air-borne foreign material. Evaporation tends to thicken the mass, and in hawking to dislodge it, some abrasion of the mucosa may occur, thus bringing about blood-streaking at times. To try to eliminate the entire production of this waste material, filtered by the nose from the inspired air, is about as sensible as to try to cancel out the function of micturition by clamping the dependent organ involved in the latter process.

The problem is especially troublesome in arid climatic zones. After suitable examination and explanation, it may help the patient to prescribe a mild spray or drop such as half and half physiologically normal saline solution and ½ per cent neosynephrine. This helps to wash out and dislodge the waste in the nasopharynx.

### Summary

Herein is reviewed a portion of the historical knowledge of the nose and its function. There are told some of the notions and misconcepts regarding the nose. Not all error has succumbed to latter-day truth. It is suggested that rhinologists bear in mind, eternally, that their primary creed must be "primum non nocere"—just as is true in all of medicine.

Note: Most informative is Proetz: Applied Physiology of the Nose. St. Louis, Annals Pub. Co.

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### A Clinical Evaluation

## of Propionyl Erythromycin Propionate\*

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A number of studies<sup>1a</sup> showed that both erythromycin and particularly its derivative erythromycin propionate have become established as an effective antibiotic. Smith and Soderstrom<sup>2</sup> obtained good results in 98 (94 per cent) patients among 105 with a variety of common infections. Side effects were mild and were found among eight patients, three of whom could not continue to take the drug.

Toxicity studies in animals disclosed no pathological findings even after large doses. Higher serum levels were obtained in animals with the ester than with erythromycin base because of its limited excretion in bile. Erythromycin propion-

ate is stable in gastric acid, thus adequate serum levels are found even in the presence of food. There has been slight or no appreciable alteration of intestinal bacterial flora. Thus gastro-intestinal disturbances have been infrequent with the use of this drug.

This report deals with our experience with both the suspension, drops and pulvules of erythromycin propionate in a wide variety of infectious diseases.

### Methods

The patient material was selected from the commonly encountered infections as seen in the outpatient department of the hospital, as well as from the private practice of the collaborating physicians. A total of 191 patients were seen by our group, among whom were 87 adults and 104 children ranging from six months to 13 years.

Infections of the upper respiratory tract and those of the urinary system are the most commonly encountered diseases and those most often seen by the practitioner. Obviously the therapy of acute and mild infections which may be transient seldom require treatment. However in the more serious

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Table I
Diagnostic Categories And
Results In Children

		No. of Patients	Satisfactory	Improved	Not Improved
1.	Upper Respiratory Inf.	(52)			
	Acute Tracheo Bronchitis " Pharyngitis	20 18	15 15	4 3	1
	Bronchopneumonia Pneumonia	5 3	3 3	ĺ	1
	Catarrhal Croup	6	6		
2.	Chronic Upper Respiratory Inf.	(6)			
	Bronchitis Asthma with infection	2 4		1 3	1 1
3.	Acute Otitis Media	8	5	2	1
4.	Acute Follicular and Lacunnar Tonsilitis	14	10	2	2
5.	Acute Sinusitis	5	3	1	1
6.	Acute Upper Respiratory Infections as a complication of Viral infection, Mea-	1.1	C	4	,
	sles, Pneumonia	11	6	4	1
7.	Influenza (Grippe)	8	1	4	3
		104	67	25	12

infections, or those that have become protracted and chronic, the use of an antimicrobial agent is indicated.

### Dosages

Adult Patients: We have used Ilosone pulvules (250 mgr) for one year. The dosage employed was one tablet three times daily, which we found was a sufficient dose for efficacious results in most of our cases. The more resistant cases were given one tablet four times daily.

Pediatric Cases: Here as well, the dosages were "tailored" to fit the patient at all times. Our purpose was to attain therapeutic response with a minimal dose and no side effects. The dosage for children was (125 mgr per 5 cc in teaspoon) one-half to one teaspoon three to four times daily, and drops (100 mg per cc) in dosages of two and one-half mg per pound per body weight three or four times daily.

No attempt was made to screen the patients for this study. They were seen by us either at the hospital, outpatient clinic, or at our offices. Those with fever and severe symptoms were seen at home.

### Results

The study was conducted for a period of one year. The patients were adults, as well as children ranging in age from six months to 13 years. Bacteriological studies of the nose, throat and, at times, of the sputum were done. When feasible and indicated, complete blood counts and urinary studies were done. The duration of therapy was from three to 14 days, depending upon the severity of illness or complications. There were recurrences of illness in two patients. In one case therapy was discontinued because of severe stomachache. Side reactions as a whole were mild. There were three cases of diarrhea and one of vomiting, and two patients with soft stools.

We saw eight patients whom we tentatively diagnosed as suffering from influenza. While the disease is endemic, even in non-epidemic years there is a high incidence of influenza infections. The disease is most often self limited and mild; in

Table II
Diagnostic Category And Results
In Adult Patients

Diagnoses	No. of Cases	Dosages	Satisfactory	Improved	Ineffecctive
Ac. pharyngitis	21	IT T.I.D.	21		
Ac. Tracheo bronchitis	6	IT T.I.D.	6		
Subacute resp. chron. pharyngitis	2	IT T.I.D.	2		
Chron, Bronchitis	1	IT Q.I.D.	1		
Chronic Asthma	3	IT T.I.D.	1	2	
Emphysema with Asthma and Bronchitis	4	(3) IT T.I.D. (1) IT Q.I.D.	1	2	1
Viral Pn	1	IT T.I.D.	1		
Ac. Cellulitis	15	IT T.I.D.	11	3	l Up- setstomach; drug dis- continued.
Otitis Media	4	(3) IT T.I.D. (1) IT Q.I.D.	4		
Ac. Laryngitis	1	IT Q.I.D.	1		
Ac. Cystitis	8	IT T.I.D.	5	3	
Ac. Pyelonephritis	8	(5) IT T.I.D. (3) IT Q.I.D.	5	2	1
Chronic Cystitis	2	IT Q.I.D.		1	1
Prostatism with infection	2	(1) IT T.I.D. (1) IT Q.I.D.		2	
Non-specific Vaginitis	1	IT T.I.D.		1	
Ac. Bartholinitis	1	IT T.I.D.	1		
Erysipelis	1	IT T.I.D.	1		
Metastatic pyrogenic abscess, furoncalesis	2	IT T.I.D.	1	1	
Thrombo phlebitis	4	(2) IT T.I.D. (2) IT Q.I.D.	2	2	
	87		64	19	4

some patients prostration, high fever and toxicity may occur. These are the result of a secondary bacterial infection, usually strep, staph, pneumo and H influenza. Bacteriological studies revealed one patient with H influenza and alpha strep, one with pneumococci, one patient with pneumococcic and H influenza. The remaining five had negative cultures.

The diagnostic category of patients and results, as well as bacteriologic studies, are summarized in separate tables. When patients responded promptly to therapy, generally within 3-4 days

(afebrile, less toxic, asymptomatic), we classified them as satisfactory results. Those that showed subjective clinical recovery, yet still manifested some objective evidence of toxicity such as fever, cough, pain, etc. after 4-5 days of therapy, were classified as improved.

Five children developed acute otitis media after a bout with measles. They all recovered within 10 days with no impairment of hearing.

The results of our investigation were gratifying among 104 children. There were 67 with satisfactory results, 26 patients improved and 11 patients

## Table III

### Culture Studies

Common Organisms Found In Normal Nose & Pharynx	Pathologic Organisms	Organisms Found in Series of Nose & Throat Cultures Done
Staphylococcus Albus B	Streptococcus Hemolyticus	Hemolytic Staph Aureus
Staphylococcus Albus A	Staphylococcus Aureus A & less B	Pneumococcus
Streptococcus Viridans	Pneumococcus	N. Catarrhalis
Diphtheroids	H. Influenzae	H. Influenzae
1	Friedlander's	Alpha Streptococcus
		Beta Hem. Streptococcus
		B. Aerogenes

### Case Reports In Brief

Pt.	Age	Diagnosis	Assoc. Pathology	Clinical Course
W.M.	3	Acute Tonsilitis	W.B.C. 17,000	T. 102.6 gradual defervescence
A.C.	10	Acute Otitis Media	Measles	T. 101.8 toxic sore throat afebrile in six days, drums N. in eight days, hearing N.
B.E.S.	4	Acute Trach. Bronch.	Hem. Staph. Aur.	T. 101 cough, toxic, afebrile in two days
H.N.	9	Upp. Resp. Inf. Sinusitis	Hem. Influenza Alpha Strep.	T. 102 cough, sore throat antra cloudy, afebrile by third day, cleared and well in 10 days
J.B.	12	Influenza Upp. Resp. inf.	Pneumo. H. Influenza	T. 103 toxic weakness headache cough muscle pain subjective improvement third day; T. 100, afebrile sixth day; well and about 10th day
D.S.	5	Acute pharyn. catarrhal croup	B. Aerogenes Hem. Staph. B. Subtilis (contamination?)	T. 101 Subjective improve. in 24 hrs. afebrile in 48 hrs., complete recovery in three days
F.S.	10 mos.	Broncho., Pn.	W.C. 14,750	T. 101.5 cough, rales, toxic, afe- brile third day, recovery fifth day
W.J.	11	Acute Trach. Bronch.		Sore throat with drip and cough, muco-purulent secretion recovery in three days
S.S	8	Acute Tonsilitis	B., Hem. Strep. Allergic to Penicillin	Severe sore throat, dysphagia T. 101.5 adenitis recovery in three days
T.J.	7	Influenza?	W.B.C. 4,970	T. 102 toxic, headachy dry cough, running nose epistaxis no improvement after three days of therapy patient treated with aspirins
T.W.	14 mos.	Upp. resp. inf.		T. 100 sneezing, running nose, malaise of three days duration improvement with drug within two days
A.P.	lyr.	URI	Wbc 14,360 Hem. Staph Aur Pneuo	T. 103 cough, sneezing, restless; recovery four days
H.G.	13	Asthma with secondary infection	Hem. Staph. Aur. Alpha strep. and non-path. Neisseria	Six year history of asthma and allergy, caught chill T . 100, wheezing, infection under control in three days

Pt.	Age	Diagnosis	Assoc. Patholog y	Clinical Course
R.A.	4	Upper Resp. Inf.	Nose Culture- Hem. Staph. Albus and A. Strep., throat showed coliform organism Alpha Strep. and Hem. Staph. Albus	Symptoms cleared within five days however three days later developed acute sinusitis which did not respond to ilosone, refr. to ENT specialist
М В.	10	Upper Resp. Inf.	Otitis Media Hem. Staph. Aur. Pneumo. and N. Catarrh.	T. 102 dry cough, nose running, right ear drum injected and adenitis, Gradual defervescence in three days, afebrile in four days, drums normal in seven days
T.P.	51/2	Pncumonia	Nephritis (?) Cystitis (?) Hem. Staph. Aur. Pneum. Allergic to Penicillin	T. 103, cough, urinary disturbance, cyclids puffy, urine two plus albumin T. 101 next day, diminished cough, urine clear by fourth day, asymtomatic 10 days
N.K.	9	Upp. Resp. Inf.	Chickenpox (?)	T. 100, adenitis, cough, Nosc clogged asymptomatic and recovery in four days
K.C.	11	U.R.I.	Bronchitis (?) Hem Staph. Aur. B. Hem. Strep. Pneumoc.	T. 101.5 cough, increased breath sounds, mucopurulent expectoration patient did well with subsidence of symptoms and pathology in five days
A.C.	61/2	Otitis Media	Measles Pneumococ. Hem. Influenza	Following measles, patient seized with severe earache bilateral, T. 103, toxic, symptomatic improvement in two days, T. 102, afebrile in four days, drums clear in 10 days, hearing unimpaired
T.S.	8	Acute Naso Pharyngitis, Sinusitis ?	Hem. Influenza Hem. Strep	T. 100.8, Adenitis, sore throat, nose clogged and running. Improved and afebrile in five days.

who failed to respond to the drug. Among the adult group, comprising 87 patients, 64 responded satisfactorily, 19 showed improvement, and treatment was ineffective among four.

We found no basic difference in clinical response between patients with positive bacterial findings and those with negative cultures.

### Comments and Conclusions

The clinical impression gained from this study is that erythromycin propionate is a useful and safe drug in the treatment of a variety of common infections seen by the general practitioner and pediatrician. The drug also showed satisfactory results in those patients who were sensitive to other antibiotics such as penicillin and the mycin drugs.

Improvement was evaluated clinically by the

remission of subjective symptoms or disappearance of inflammation, fever and other signs of infection. There was a noticeable paucity of untoward reactions. No cases of fungus or allergic manifestations occurred.

As can be readily seen from a perusal of the tables, the therapeutic results were particularly more gratifying in bacterial infections such as pneumonia, otitis media, streptococcus, pharyngitis, tonsilitis, cellulitis, pyelonephritis, etc. than those due to viral origin such as U.R.I., influenza and croup.

Brief summaries of typical cases are submitted.

E.J.C. 45 yrs.m. Acute pharyngitis with ulceration of pharynx wall. Pain on swallowing for one week. Sensation of tightness in throat. Got two injections of penicillin and

terracyclin before without result. 5/4/59: Ilosone 250 mg. t.i.d. 5/7/59: Ulcers almost disappeared. Patient feels better. 5/12/59: Throat essentially improved. He received local treatment with AgNo 3 5 per cent once.

S.M. 35 yrs. f. 5/6/59: Throat infection associated with infected pouches in tonsil area. Endergland right side neck. Ilosone 250 mg. t.i.d. 5/10/59: Throat, pouches, and gland all healed.

**L.H.** 7 yrs.m. *Sore*, throat had developed on top of virus infection of throat after several days. One pus pocket on right tonsil. Tetracyclin unsuccessful. 5/12/59: Ilosone 250 mg. t.i.d. Condition cleared up after two days with fall of temp. Drug well tolerated.

V.J. 52 yrs.f. Infected foot after accident. Ulcer near metatarsal five laterally. Large area of foot is swollen, area around ulcer bluish discolored, ulcer is oozing. Under Ilosone 250 mg. q.i.d. given during one week. Condition improved, although final healing of ulcer took several weeks.

C.H. 63 yrs.f. Suffered from *U.R.I.* with coughing spells for nine days. Penicillin and tetracyclin did not clear up infection. Whitish yellowish expectoration continued. Cleared up after Ilosone 250 mg. t.i.d. Treatment started on 5/14/59.

M.E. 22 yrs.f. 5/10/59: Unspecific vaginitis which had not completely cleared up after local treatment with Tricofuren cream. Ilosone 250 mg t.i.d. given during three days was effective.

T.M. 25 yrs.f. Acute cellulitis underneath chin bone middle section possibly caused by an infected tooth. 9/5/59: Ilosone 250 mg. t.i.d. was started. 9/10/59: Infection is under control. Associated gland diminished in size and not tender.

L.M. 74 yrs.f. 12/3/59: Throat infection with tickling throat for two months. Ilosone 250 mg t.i.d. effectful in four days.

W.D. 32 yrs.f. Recurring sore throat. On 11/3/59 with difficulty of swallowing, burning sensation in throat. Patient informed me that she is allergic to most of the antibiotics, such as tetracyclin, etc. which cause inflammation in mouth and vaginitis. Ilosone was started with satisfactory result and without allergy reaction. On 11/18/59 she again developed a sore throat. She was started on Ilosone again. Treatment was successful again with no recurrence.

G.J. 57 yrs.m. 12/10/59. Upper respiratory infection with scattered ronchi through lungs. Throat slightly inflamed. Patient suffers from ragweed hayfever during the months of Aug. and Sept. Ilosone 250 mg. t.i.d. satisfactorily cleared up condition.

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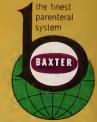
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1 Miller, E. D., Jr., and Roffer, G. W.: M. Times 89 196 (Feb.) 1961. Indications and effects: The clinical indication for Orinase is stable diabetes mellitus. Its use brings about the lowering of blood sugar; glycosuria diminishes, and such symptoms as pruritus, polyuria, and polyphagia are alleviated.

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Contraindications and side effects: Orinase is contraindicated in patients having juvenile or growth-onset, unstable or brittle types of diabetes mellitus; history of diabetic coma, fever, severe trauma or gangrene. Side effects are mild, transient and limited to approximately 3% of patients. Hypoglycemia and toxic reactions are extremely rare. Hypoglycemia is most likely to occur during the period of transition from insulin to Orinase. Other untoward reactions to Orinase are usually not of a serious nature and consist principally of gastrointestinal disturbances, headache, and variable allergic skin manifestations. The gastrointestinal disturbances (nausea, epigastric fullness, heartburn) and headache appear to be related to the size of the dose, and they frequently disappear when dosage is reduced to maintenance levels or the total daily dose is administered in divided portions after meals. The allergic skin manifestations (pruritus, erythema, and urticarial, morbilliform, or maculopapular eruptions) are transient reactions, which frequently disappear with continued drug administration. However, if the skin reactions persist, Orinase should be discontinued.

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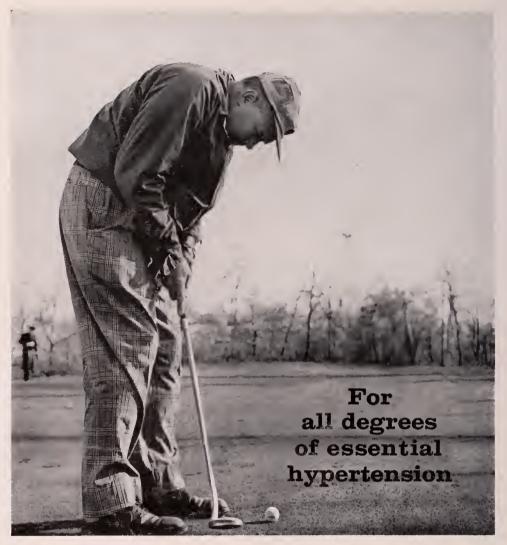
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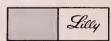


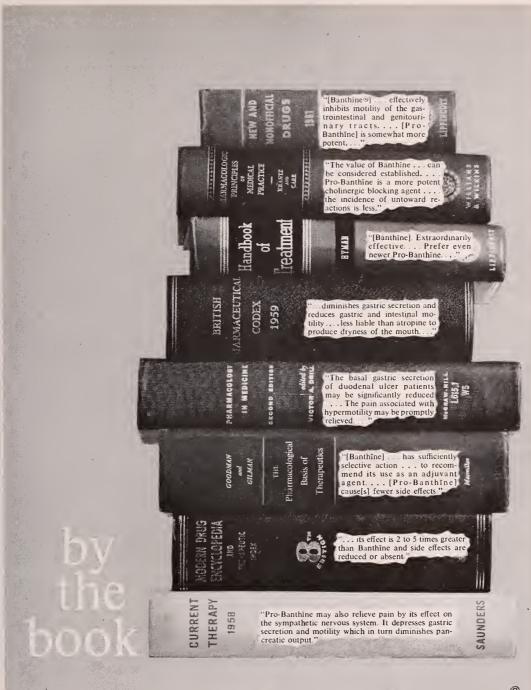


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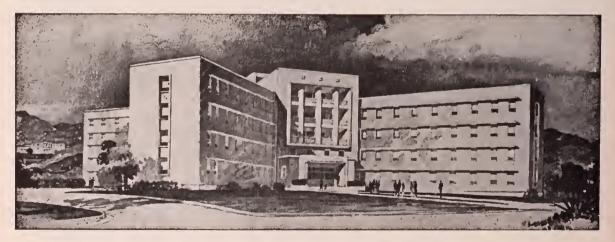
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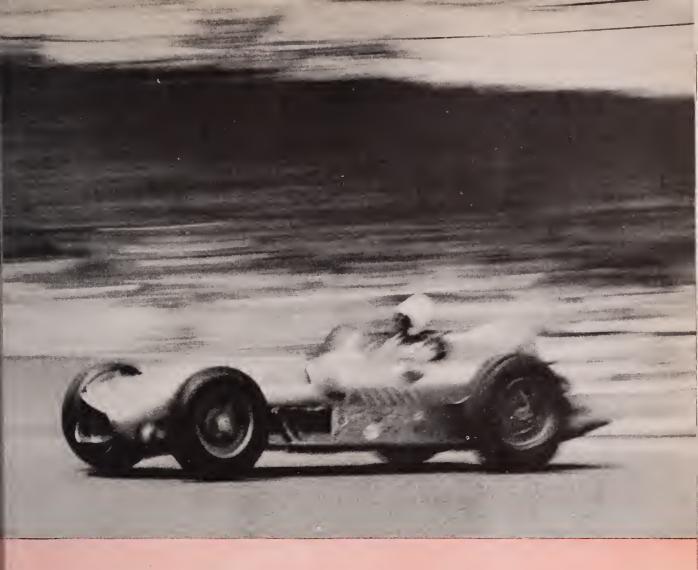
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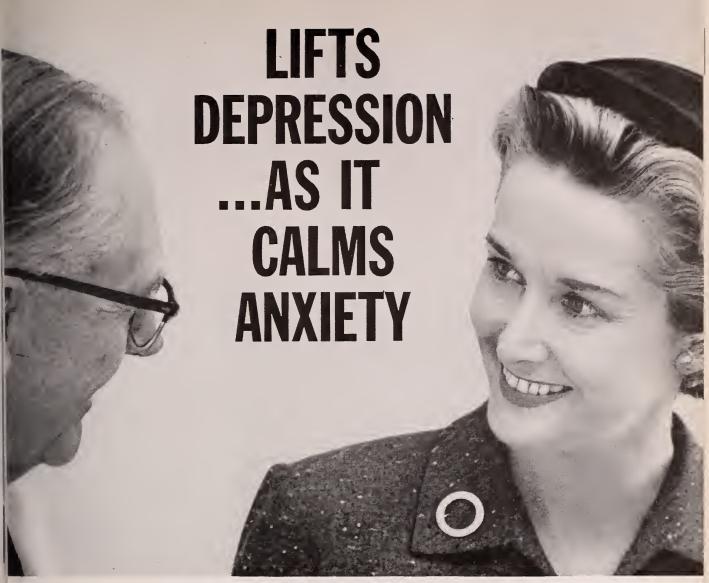
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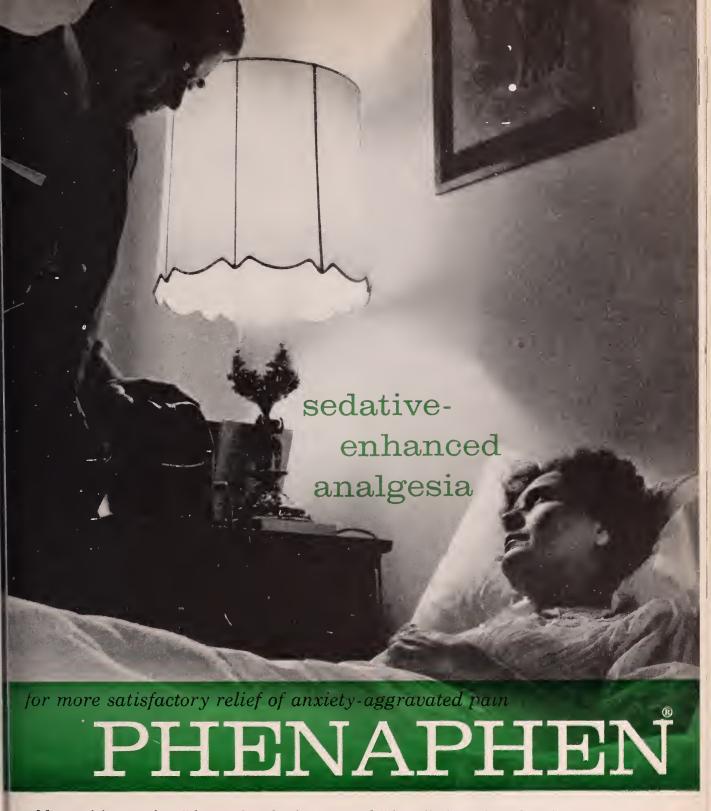
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Meyers, G. B.: Ind. Med. & Surg. 26:3, 1957.
 N. Y. St. J. Med. 53:1867, 1953.

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1. Hodges, F. T.: *GP* 14:86, Nov., 1956. 2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

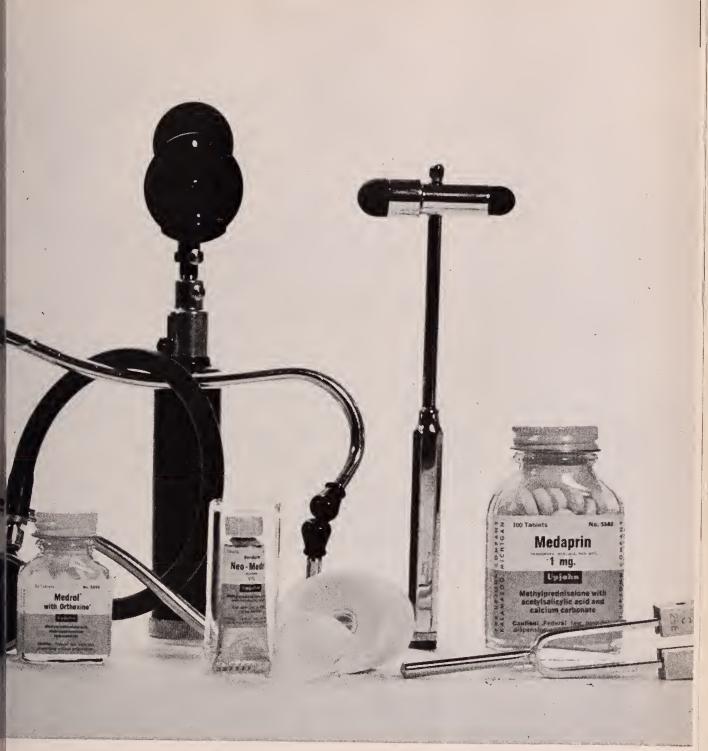
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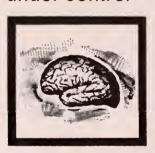
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### Depression and Psychosomatic Illness\*

WILFRED DORFMAN, M.D.,\*\* Brooklyn, N. Y.

Depression can be firmly integrated and interwoven with all types of somatic illness and is not limited to specific psychosomatic disorders. It may precede, co-exist, follow or alternate with the somatic difficulties. It can be overt, obvious, and offer no difficulties in recognition; it can also be covert, concealed and masked by the somatic symptoms.

In peptic ulcer, specific oral dependency needs are postulated by Franz Alexander<sup>1</sup>. This dependency led Garma<sup>2</sup> to the picturesque speculation that the ulcer patient introjects the needed mother figures and then "bites" and ulcerates his gastric mucosa. Ambivalence, aggression, retroflexed rage, and self-punishment — all features of depression—seem evident.

Perhaps the retroflexed hostility is related to some dim awareness that he has swallowed too much; nevertheless, the eventual ulceration seems to make provision for dependent needs to be at least symbolically fulfilled, since no single procedure, short of gastrectomy, will provide as much relief as does milk—even though it is bottled.

But if he suffers along without the need for drastic surgery, periods of depression often coincide or alternate with ulcer activity. Perhaps both reflect dependent needs which are repressed and denied.

In ulcerative colitis there is frequently an apathy not unlike that of schizophrenia. When a true depression exists it can often be correlated with difficulties in the handling of anger. Needs for love and approval make it difficult for the colitis patient to orally express normal quantities of aggression.3 The forces of repression prevent the recognition of basic hostility, despite the clear connotation of its anal delivery to everyone else.

But perhaps the diarrhea can be equally or better related to the physiological lesion than to its hostility drainage potentialities. At any rate surgical rather than psychiatric intervention may be indicated in some instances. The correction of the somatic illness may even clear up reactive depressions related to the chronic disability of ulcerative colitis.

### Obesity

In obesity, food and love are equated. Food is used to supply narcissistic needs, so that the development of obesity may represent a futile attempt to fill an emptiness that is misinterpreted as hunger.4 Many obese patients become depressed when they begin a weight reduction regimen. This can occur with or without anorexigenic medication; unfortunately, it can also occur after the weight reduction is fairly successful.

Perhaps it is in order to avoid depression that many so quickly regain their hard-earned losses. At any rate, it is evident that in many overweight patients, the obesity serves as a wall of defense. The penetration of this barrier without adequate handling of the psyche is often fraught with danger.<sup>5</sup> Acute depression or acute schizophrenia may result. The fact that so many obese patients can be reduced without a psychiatric detour simply indicates that all obese patients are not alikedespite external and quite superficial resemblances.

In hypertension, a calm outer facade may hide a turbulent internal milieu. Too often minimal aggression is displayed, due to the fear of loss of love and its symbolic equivalents. With the use of reserpine and some of its derivatives, the hypertension will often recede, but in its wake there often appears symptoms of tiredness, discouragement and depression.

Some observers 6 have noted that the depression may not be a "true depression", but is often

<sup>\*</sup>Presented at a Panel Discussion, Brooklyn Psychiatric Society, March 15, 1962. \*\*Departments of Psychiatry and Medicine, Maimonides Hospital of Brooklyn; Faculty, Department of Psychiatry, Downstate Medical Center, New York.

better related to the effects of tranquilization in a personality who is threatened by passivity. In some instances, however, a true depression does result which may be severe enough to warrant ECT. Recent biochemical advances have traced this reserpine-induced depression to a lowering of serotonin and norepinephrine. From a psychodynamic point of view, the lowering of the blood pressure removes an outlet for aggression. Retroflexed hostility and the resulting depression may perhaps represent the psychodynamic concomitants of the biochemical effects of a lowering of these amines.

The alternation of hypertension with depression reminds me of a patient with severe hypertension (300/160) whom I finally convinced to undergo a Smithwick splanchnicectomy many years ago, when I was a vigorous and enthusiastic internist. Her blood pressure promptly dropped to normal levels but she soon became so severely depressed that she required hospitalization in a mental hospital. Fortunately, the operation failed. When her blood pressure rose, so did her spirits, and she recovered.

### Coronary Disease

Coronary disease, especially a recent occlusion, should produce a normal reactive depression in anyone who understands the life history of this disease. In those who have a driving compulsive need for success, whose ego function becomes severely disturbed by the crippling effects of the disease, the loss in self-esteem may increase the severity of the depression.

Perhaps, a defect in ego function permits this compulsive defense to become established; when genetic vulnerability (poor vascular tubing) and metabolic dysfunction in the handling of cholesterol and other lipids are added, the stage may then be set for early coronary disease.

In diabetes mellitus, as in obesity, the need for love and the need for food can be synonymous. The discovery of diabetes is a frequent precipitating factor for reactive depression; chronic uncontrolled diabetes, as with any chronic illness, can produce chronic depression. Some studies have indicated that common genetic factors may exist in diabetes, gout and depression, so that the anlage for depression may be present long before its appearance.

Diabetic patients, like obese patients and many other mortals, are often happiest when they are permitted to eat without restrictions. Diabetic diets that are severe and aim for complete chemical control do not necessarily produce a longer life—although to many starved and orally deprived patients it certainly seems to be much longer due to a chronic depression.

Bronchial asthma, with its often found pattern of intense dependence upon the mother, where the attack is often produced by actual or symbolic separation, may in some instances be an alternative to depression. As with other psychosomatic diseases, this alternation is by no means a constant finding, but is related to the individual personality. Ego strength, the secondary gain of illness, the amount of support provided while the defenses are removed, are all important factors.

### Rheumatic Disorders

Rheumatic disorders, inclusive of arthritis, fibrositis, low back pain and painful disc syndromes, may produce depression due to somato-psychic effects. In addition, there is evidence pointing to the role of repressed aggression in many patients with rheumatoid arthritis. Here, too, the disease may be an alternative to depression.

In other patients the depression may be concomitant with the disease-a somatopsychic effect of chronic suffering pain and disability. Too often, in the recent past, the use of corticosteroids has mobilized arthritics only to produce severe emotional repercussions. In many, sensitized by their premorbid personality, depression followed in the wake of sudden liberation from the protective restrictions, defenses and secondary gain produced by the disease.

Some dermatologic conditions — especially neurodermatitis, may also be concomitant or alternate with depression. Many investigators have emphasized the importance of repressed rage and guilt in various psychocutaneous excoriation syndromes. <sup>7,8</sup> That skin disease can alternate with depression in some individuals is evident when one reviews some of the results with corticosteroids. Here too the premorbid personality is usually more important than the pharmacological effects per se, except that on occasion a lowering of the serum potassium can produce psychiatric sequelae.

Depression, in all of these psychophysiologic and conversion reactions, may be overt and obvi-

ous or covert and hidden. If overt, there is usually no problem in its recognition, unless the physician is preoccupied with the somatic symptoms and/or disease. It may therefore take considerable time before he can stop his often obsessive-compulsive repetition of laboratory and other studies.

Too often it is only when the doctor's ego is threatened by impending therapeutic failure that he suddenly becomes aware that his patient may have emotional difficulties and require psychiatric opinion or referral. As for the masked or covert depressions, these naturally evade diagnosis even longer.

The psychiatrist rarely sees these patients unless he serves in a general hospital or is particularly interested in patients with psychophysiologic illness. It is obvious that these patients can successfully evade and avoid psychiatric intervention, since the repression which produced the psychophysiologic illness is maintained by denial at both conscious as well as unconscious levels.

### Treatment

The treatment of the depression will be influenced by two major factors: 1) the nature of the depression, 2) the philosophy, training, orientation and convictions of the therapist. Electroshock, psychotherapy, pharmacotherapy all have their proponents, exponents and opponents. Neurotic or reactive depressions are best handled by psychotherapy.

In a few of these instances, antidepressants may be synergistic with psychotherapy and make for greater accessibility. Psychotic depression — whether endogenous, manic depressive or involutional, is usually best treated by electroshock and/or pharmacotherapy, followed by psychotherapy. At times, some of the newer drugs can eliminate ECT or at least cut the number of treatments considerably.

These newer drugs include the amine oxidase inhibitors (phenelzine, isocarboxazid, nialamide, tranylcypromine) as well as the non-MAO, imipramine and amitriptyline. The MAO inhibitors and imipramine seem to work best in purely retarded states. Amitriptyline is preferable when high levels of anxiety accompany the depression.<sup>9</sup>

In many instances, the use of these newer pharmaceuticals can make the patient more amenable to psychotherapeutic management. This is especially valuable in many severe psychotic depressions where heretofore only ECT was available. With drug therapy and fewer, or no ECT, the patient suffers no iatrogenic confusion state and can work with the therapist in an attempt to get to the roots of the difficulties and possibly produce changes in basic attitudes.

As for psychotherapy, it has been repeatedly emphasized that "psychosomatic" patients show poor results. One should differentiate here between those who can be motivated for psychotherapeutic exploration and those who persistently cling to their defense of denial of emotional difficulties. It is in this latter group, which includes the "masked" depressions, that combinations of drug and psychotherapy can increase the patient's accessibility. <sup>10</sup>

Whether this increase is due solely to biochemical influences or to the fact that the therapist is now meeting the patient's need for "oral supplies" in the form of drugs, is indeed difficult to evaluate. Attempts to differentiate between these two effects are often fruitless and produce considerable consternation in statisticians, biochemists, pharmacologists and double-blind enthusiasts who quite logically strive for a scientific approach.

These attempts strike at the very roots of the body-mind dilemma. Psyche and soma, fortunately for both, are well attached. This situation will persist, despite the fact that specialized training seems to require that there not only be a split, but a constant subdivision of each of them into smaller and more comfortable compartments.

### 1921 Newkirk Avenue

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# Postoperative Peritonitis Simulating an Abdominal Catastrophe

Report of Two Cases

C. HERBERT FREDELL, M.D.,\* Flagstaff, Ariz.

During the early postoperative period following abdominal surgery, the surgeon finds it difficult accurately to assess abnormalities within the abdominal cavity. Complications of surgery are not always manifested in a typical manner during this time.

Peritonitis is a postoperative complication that should be avoided. In spite of early accurate diagnosis, careful surgical technique, and a multitude of antibiotics, this complication is still associated with a high mortality rate.<sup>1</sup>

Peritoneal irritation of a varying degree occurs following most intra abdominal procedures. It may be a mild localized type due only to the surgical incision and the visceral manipulation or it may be more extensive with typical signs and symptoms accompanying it. The latter situation usually requires time to develop and can usually be anticipated.

Its onset is gradual and discernible. Frank<sup>2</sup> observed that the development of acute peritonitis in the postoperative period may be signalized by the onset of vascular collapse without recognizable abdominal signs. He emphasized that the role of infection in producing shock must not be underestimated on the basis of absence of signs and symptoms of inflammation.

In recent years the author has had two similar cases of early postoperative peritonitis which have illustrated this uncommon sequence of postoperative events.

### Case No. 1

A 51 year old white male was admitted to the Flagstaff Hospital on Feb. 2, 1957, complaining of cramping generalized abdominal pain accompanied by intermittent vomiting of four days duration. He had been passing flatus freely but had no stools.

His past history revealed that he had a left hemicollectomy for diverticulitis with abscess and obstruction of the descending colon in September 1956.

Physical examination revealed a soft tympanitic distended abdomen with hyperactive high pitched bowel sounds.

Laboratory examination revealed a white blood count of 15,000. Roentgenogram of the abdomen revealed several dilated loops of small intestine.

A Levin tube was placed in the stomach and fecal colored material was obtained. He was given intravenous fluids and remained on constant nasogastric suction for four hours. A laparotomy was then done.

There was a volvulus of the ileum involving ten feet of gangrenous appearing intestine. After the adhesive band was divided, and the volvulus re-

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duced, viability rapidly returned to the involved intestine. A bowel resection was not done.

Twenty-four hours postoperatively, the patient was sitting on the toilet attempting to pass flatus when he experienced sudden severe abdominal pain near the umbilicus. He promptly went into shock and was very cyanotic. His temperature was 101 degrees F. rectally. A chest roentgenogram, electrocardiogram and hematocrit were done revealing no abnormality. It was felt that he had a mesenteric vascular occlusion and that early re-exploration should be done.

He was given vasopressors, blood, and massive intravenous antibiotics with prompt return of the blood pressure to normal limits. Exploration then was done through the previous incision. A massive fibrinous peritonitis with a moderate amount of cloudy intraperitoneal fluid was found. The bowel was viable and there was no perforation.

Following the second laparotomy, his clinical course was a stormy one. He was febrile to levels of 106 degrees F. and markedly hypotensive. He required massive doses of Levophed for seven days postoperatively. He was anticoagulated with heparin and given massive doses of tetracyline.

On the third postoperative day he had roent-genographic evidence of a right lower lobe pneumonia. At this time he became icteric. Two days later a wound infection was apparent which was due to pseudomonas aeruginosa and B hemolytic streptococcus. Sensitivity studies revealed chloro-ampheticol to be the drug of choice. This was given in double the usual recommended dosage.

On his sixth postoperative day he had a violent bout of coughing and had a complete dehiscence of his wound. Due to his critical condition only tamponading of the wound was done. His fever fell shortly after this and he maintained his blood pressure with no vasopressors. He had a normal stool and good oral intake by his tenth postoperative day.

On his eleventh postoperative day, a massive monilia albicans infection of his oropharynx and anus was evident. Mycostatin was given and the antibiotics were discontinued with prompt improvement of that problem. On his twenty-third postoperative day he was discharged from the hospital fully ambulatory with a granulating wound of his abdominal wall.

Follow up examination six months later revealed a healed soft incision with a ventral hernia two by three inches in diameter which was well controlled by an abdominal belt.

### Comment

This case of volvulus of the small intestine was due to postoperative intrapertioneal adhesions. Following lysis of the adhesions, an acute severe peritonitis occurred. The massive contamination due to the temporary ischemia of the intestine was not fully appreciated at the time of surgery. The sudden onset of shock without signs of infection lead to the erroneous conclusion that some catastrophic episode such as mesenteric thrombosis had occurred.

The clinical course postoperatively was a stormy one with near fatality occurring on more than one occasion. The intensive prolonged vasopressor therapy that was required was unusual. The patient's condition improved markedly following the evisceration. This is not a recommended measure in the management of this type of problem.

#### Case No. 2

A 67 year old male who appeared older than his stated age was admitted to the Flagstaff Hospital on Nov. 5, 1959, complaining of generalized vague upper abdominal pain and distention for the preceding week. He was anorexic but had no nausea or vomiting. He noted that the pain had become more severe during the twenty-four hour period prior to admission.

Physical examination revealed tenderness and involuntary abdominal muscle spasm in the right lower quadrant.

The white blood count was 14,000 with a normal differential smear. The stool was positive for occult blood.

Exploration of the addomen was done on Nov. 5, 1959, expecting to find acute appendicitis. The appendix was normal in appearance. Examination of the entire gastrointestinal tract revealed no abnormality. There was no apparent cause for his abdominal complaints.

Postoperatively, he complained of persistent abdominal pain about his umbilical region and remained distended. He had repeated emesis and did not pass flatus. On his sixth postoperative day his distention was more marked and the emesis was fecal colored. Roentgenograms at this time revealed distended loops of small intestine with fluid between them. It was felt that he had intestinal obstruction due to vascular insufficiency.

The right rectus incision was reopened and five feet of gangrenous upper jejunum due to mesenteric thrombosis was found and removed. A jejunostomy was done.

He did well until forty hours postoperatively, when he complained of sudden severe upper abdominal pain and went into profound shock.

The hematocrit was 49 mm. Wintrobe; the electrocardiogram did not reveal any abnormality. His temperature was 102 degrees F.

It was felt that he had sustained another mesenteric thrombosis or that the anastamosis had leaked. He was given vasopressors and massive intravenous antibiotics.

After he was normotensive, the right rectus incision was reopened and the abdominal cavity was explored. A massive fibrinous peritonitis was found. The anastamosis was intact. The culture was found to be a B hemolytic streptococcus, hemolytic staphlococcus aureus, and E. coli. All of the organisms were sensitive to chloroampheticol. He was given large doses of chloroampheticol, anticoagulated, and placed on intravenous vasopressors.

During the next two days he had parenteral fluid and electrolyte replacement calculated to correct his deficits and maintain an adequate urinary output. His serum sodium and potassium were within normal limits and his hydration was good, even though his hematocrit was 76 mm. Wintrobe on the second postoperative day. A phlebotomy of 750 cc of blood was done and his intravenous fluid intake was increased.

Within four hours of this change in the management, the hematocrit was 62 nm. Wintrobe and he appeared improved. Shortly afterwards he went into congestive heart failure with pulmonary edema. He was given intravenous digitalis, diuret-

ics, and positive pressure oxygen with brief improvement.

He was noted to be oliguric for the following six hours and his pulmonary edema recurred. He expired in congestive heart failure a few hours later in spite of all therapy. An autopsy was performed. It revealed a markedly arteriorsclerotic patient with all of the gross findings of congestive heart failure and massive peritonitis.

### Comment

The clinical course of this case was not obvious most of the time. Postoperatively the diagnosis was not suspected until frank gangrene of the intestine had occurred.

The sudden onset of severe upper abdominal pain and shock in the early second postoperative period was perplexing. Only his fever of 102 degrees F, was indicative of infection.

The finding of only a massive peritonitis was not expected. The postoperative course following the third exploration was complicated by his arteriosclerotic heart disease and the marked demands made upon him by his disease process. The rapid progression of the severe peritonitis had altered his extracellular fluid compartment markedly.

An effort to correct the deficit during the early postoperative period was met with the rapid expansion of the fluid compartment when the "third space" of the peritoneal cavity began to empty into it. This produced a circulatory load beyond the capacity of his chronically diseased heart.

### Discussion

Infections occur in the peritoneal cavity following intra abdominal surgical procedures that are mild enough that they will pass unnoticed during the postoperative period. More extensive infections usually will be recognized after a varying period of time and respond to antibiotics and selective drainage procedures. Massive infections occur postoperatively and usually will make themselves known over a short time and will require intensive diligent therapy to prevent demise. Less commonly, one finds a vascular collapse the first indication of massive infection during the postoperative period. When shock occurs, which is due to infection, regardless of location, the surgeon is confronted with a disease that has a high mortality rate.

It is the author's impression, after discussing this problem with several other surgeons, that it is not commonly appreciated and accurately diagnosed. The sudden onset of shock in the early postoperative period lead the author to erroneous diagnoses on two occasions. An avoidable laparotomy was done in each instance.

### Summary

- 1. During the early postoperative period it is difficult accurately to assess abnormalities within the abdominal cavity.
- 2. Peritonitis in the early postoperative period first may be identified by the onset of vascular collapse without recognizable abdominal signs. Fortunately this is not a common circumstance.

- 3. The role of infection in producing shock must not be underestimated on the basis of absence of signs and symptoms of inflammation.
- 4. Two cases of early acute postoperative peritonitis which presented a sudden severe abdominal pain with rapid onset of shock have been presented. The surgeon was misled by the signs and symptoms to the extent that laparotomy was done in each case. Both operations might have been avoided had there been a greater awareness of this manifestation of acute early peritonitis.

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### Dr. Bornstein Cited As Forensic Sherlock

Dr. Frederick Bornstein of El Paso, El Paso police medical examiner, was one of several medical criminal investigators, named in an article in the Washington Post of Sunday, March 11, 1962. The full page article was written by Reporter Nat Haseltine and describes a variety of crimes which were solved with the assistance of forensic medicine.

Dr. Bornstein's is described as "The Strange Case of the Electrocuted Baby." In this case Dr. Bornstein demonstrated that a baby alleged to have been electrocuted by accident had in fact been deliberately electrocuted by the baby's stepfather, who was subsequently sent to the Texas State Hospital for the Criminally Insane.

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### Fluprednisolone in Allergy

### A Study of 60 Patients

WILLIAM C. GRATER, M.D., Dallas

Corticosteroids are well established in the therapy of allergic disorders. The various presently available preparations, in adequate dosage, all give about 85 to 95 per cent successful results. But at these dosage levels, the spectrum of undesirable side effects has been found to differ from one derivative to another. While efficacy may be determined readily, the spectrum of the side effects requires thorough clinical trial over an extended period.

It is the purpose of this paper to report on the efficacy and side effect-spectrum of a new corticosteroid, fluprednisolone\*, after over two and one-half years' use, and thus to extend the reported experience of others.<sup>1,3</sup>

### Materials and Methods

Fluprednisolone (6-alpha-fluoroprednisolone) is a new corticosteroid analogue. It was supplied first as 2.0 mg. tablets, later as 0.75 and 1.5 mg. ones.

Sixty private patients were studied for periods of treatment ranging in length from two weeks to two years. Emphasis was placed on choosing patients with long-term steroid requirements; 39 were already on maintenance therapy when shifted to fluprednisolone. The remaining 21 patients had one or more acute allergic disorders requiring only short term administration. In Table 1 may be

seen the various clinical allergic manifestations presented.

It should be noted that these patients were atopic or allergic. Constitutionally, they differed from rheumatoid ones, having less of a tendency toward osteoporosis or to peptic ulceration as a part of the natural course of their untreated disease. They further were different in that maintenance dosages often may be quite low as compared to the amounts required in, for example, rheumatoid arthritis.

Yet allergic patients may be entirely suitable for milligram-for-milligram comparisons of different steroids. Given an intractable asthmatic on maintenance steroid therapy, pulmonary function may be determined and the patient shifted to a new analogue. The lowest dose then required to maintain the same pulmonary function is the equivalent dose.

Another useful device was to measure objectively the degree of mooning of the face, by placing a tape just below the nose and under the ears.

### Results

### A. Dosage Equivalence

Eleven patients receiving an average daily dose of 8.9 mg. of prednisolone were shifted to fluprednisolone. Maintenance dosage was then 4.1 mg. per day. Similarly, 15 patients originally maintained on 5.5 mg. of methylprednisolone, on

<sup>\*</sup>The Upjohn Company trade name, Alphadrol.

Table 1.

The 96 Clinical Allergic Conditions
Noted Among 60 Patients

DISORDER	TIMES	NOTED
Allergic rhinitis		28
Allergic conjunctivitis		
Asthma		47
Urticaria		1
Drug reactions		7
Contact dermatitis		3
Atopic eczema		6
		96

the average, required 3.0 mg. of fluprednisolone.

Fourteen who needed an average of 1.2 mg. daily of dexamethasone required 3.4 mg. of the new corticosteroid. By coincidence, 3.4 mg. was also the average requirement among the whole group of 39. (One patient had previously been titrated both for prednisolone and dexamethasone and was entered in both groups of comparisons, thus bringing the total to 40.)

### B. Results of Therapy

Among the 96 allergic manifestations listed in Table 1, satisfactory results were obtained in 89 (93 per cent). An example of excellent response may be seen in the photographs. Four asthmatics, two patients with atopic eczema and one with allergic rhinitis had outcomes considered as unsatisfactory.

Objective evidence of improved pulmonary function in patients with asthma has been set out in Table 2. Significant improvement was noted in all patients but one (E. W.), especially for the half second vital capacity.

### C. Side Effects

No major side effects were encountered during this study, nor were new or unusual ones noted. One patient complained of headache, one of nervousness. Three developed mild-to-moderate moon facies, one having been maintained on the drug, 1.5 to 3.0 mg. daily, for two years. Of 12 cases of moon facies which had developed while other steroids were being used, seven improved markedly after they were shifted to fluprednisolone.

This steroid appeared to have less tendency to increase appetite, weight gain and abnormal deposits of fat than prednisolone or methylprednisolone. It was free of the induction of abdominal discomfort and psychic stimulation, symptoms occasionally associated with administration of dexamethasone. And no tendency to muscle weakness, weight loss or depression, side effects associated with the use of triamcinolone, was observed.

From a practical view point, these advantages are not too significant in short term therapy but may be of considerable importance in long term maintenance.

### Summary and Conclusions

Fluprednisolone (6-alpha-fluoroprednisolone) was studied in 60 private patients with allergic disorders as initial therapy (21) or after maintenance on one or more older steroids (39 patients). Of the 96 allergic manifestations they presented, 89 responded satisfactorily (93 per cent). Length of treatment varied from two weeks to two years.

Table 2. Pulmonary Function Changes in Patients with Asthma Following Fluprednisolone

Pt.	Half Second Vital Capacity		Total Vital Capacity	
	Before Therapy, M.L.	After Therapy, M.L.	Before Therapy, M.L.	After Therapy, M.L.
JH	2800	2800	3600	3800
OJR	2700	3000	4400	4600
JB	800	1300	2200	2300
MK	700	1300	1500	2500
EJ	1700	2100	4000	4600
EW	1200	1200	4000	3900
JP	400	500	1400	2000
ВВ	400	1200	1200	1900
AV.	1338	1675(+25%)	2788	3200(+15%)



Figures 1A, 1B

Patient V.T., presented with a dermal reaction of hypersensitivity to hydroxychloroquine, Figure 1 A shows appearance of lesions on upper chest prior to fluprednisolone. After discontinuing the offending drug and five days' treatment there was complete clearing (Figure 1 B).

Milligram-for-milligram comparisons showed that fluprednisolone was about 2.2 times as potent as prednisolone, 1.8 times methylprednisolone and approximately 0.28 times dexamethasone.

Side effects noted in five patients were headache, nervousness, each in one subject, mild-tomoderate mooning of the face in three others. Patients were conspicuously free from the following: increased appetite, weight gain, abdominal discomfort, psychic stimulation, muscle weakness, weight loss, and mental depression.

These advantages may be of considerable importance, especially in patients requiring long term maintenance therapy.

1620 Medical Arts Building

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### Chest Physicians to Meet in June

The American College of Chest Physicians will hold its five-day annual meeting at the Morrison Hotel, Chicago, June 21-25.

The scientific program will include postgraduate seminars, open forums, a cine symposium, round table luncheon sessions, and motion pictures and will cover such topics as tuberculosis, underwater physiology, chest roentgenology, cardio-pulmonary

trauma, histoplasmosis, congenital heart disease, and cardiac surgery.

On Monday, June 25, there will be a joint meeting between the American College of Chest Physicians and the American Medical Association at McCormick Place, Chicago's new convention center.

### Letters to the Editor

The following letters have been received by the Editor of SOUTHWESTERN MEDICINE and are self-explanatory.

### New York Obstetrician Criticizes Article on Pregnancy Weight Controls

The Editor Southwestern Medicine

Dear Sir:

I have just read the article by Campbell and Gorman entitled, "Clinical Evaluation of Weight Control During Pregnancy" published in your July issue. (42:7, July 1961)

May I say that these authors are to be congratulated upon their interest in the control of weight gain, a subject which at present attracts so much lay and medical attention. During pregnancy the incidence of stillbirth and neonatal death, preeclampsia, increased fetal size and post-partum hemorrhage, as well as other complications, is much higher in the overweight. For this reason it is of paramount importance that as much accurate data as possible, collected by responsible investigators, should be disseminated to the profession.

We have been interested in the problem of weight control and obesity for a number of years (Ref. 1,2.) and have already collected a series of over 400 treated cases of excessive weight (180-350 lbs.) during pregnancy. In view of this our interest in the above paper is easily understood, particularly since the authors discuss and define obesity and its diagnosis at great length, even though the cases which were treated were not obese.

### Weight Control

However, I could find no indication of weight control in their article. They seem to have taken patients of normal average "prenatal" weight (I assume they mean pre-gravid) and found them to have remained within the average range of normal pregnancy weight increment, after treatment. Their Group "A" patients (136 lbs.) gained twenty pounds during pregnancy and their Group "B" cases (139 lbs.) gained a similar amount. Their controlled Group "C" (145 lbs.), treated with diet alone, gained thirty pounds. To be exact, Group "B" treated with amphetamine actually showed a lesser weight increment than Group "A" treated with a "low calorie candy-type vitaminmineral agent." None of the three groups showed a total increment outside the average normal range. (Ref. 3,4.) When evaluating the effectiveness of a particular form of therapy would it not be a much more rational procedure to use an untreated group as a control?

In view of all the above I am at a loss to see where the treatment described, particularly the candy-type agent, controlled weight.

### **Blood Sugar Levels**

The control of weight gain by elevating blood sugar levels, so that function of the hypothalamic satiety center is inhibited, may be all right in the non-pregnant state. However, it is certainly a novel approach during pregnancy. The general consensus is that pregnancy is a diabetogenic state (Ref. 5) and it is universally recognized that the characteristic symptom of diabetes is hyperglycemia. One might ask whether the undetected pre-diabetic, subjected to 32 weeks of artificially raised blood

sugar, as the patients in this study were, might be adversely affected? Do you not agree that practitioners who might be prompted to use the product described (Ayds) should be made aware of the above possibilities? One might also ask whether the patients treated with this material were investigated, in order to rule out diabetes, before therapy was started.

I was interested in another novel thought advanced in this paper. The authors state that "liquid diets are contra-indicated during pregnancy because they contribute to an increase of body fluid." One can only assume that they wished to convey the impression that this type of diet leads to increased water retention.

### Liquid Diet

If this is accepted it would deprive the pregnant woman of one of her most dependable forms of liquid diet in the form of milk. At least one quart daily intake is advocated by all authorities and the benefit of this liquid diet is hallowed by time, usage and experience. It has not been found to have any deleterious effects upon body fluid, nor has any other form of liquid diet employed at the present time. In our clinic, we have treated over 90 cases of obesity (180 lbs. plus) with a daily quart of metrecal and in no instance have we observed any effect of this upon body fluid. We are on the lookout for this phenomenon because of extensive experimental work with oral diuretics. Alteration in the amount of body fluid, in a pregnant woman, is not a factor of fluid intake. Fluid retention is a physiologic feature of pregnancy and is now known to be a manifestation of the hormone picture. As much as six liters may be normally retained in order to serve the additional needs of both the mother and the fetus. It is only when fluid retention becomes excessive, for reasons still unknown, that the need arises to control fluid intake. In treating patients with excessive water retention we have not found it necessary to concern ourselves with the fluid in the diet if adequate diuretic therapy is used. In the paper under discussion there was no mention of excessive fluid retention in any case, and I wonder upon what basis the authors make this rather daring statement regarding liquid diets. Because of our interest in this field it would certainly be important for me to know whether any of their patients were treated with this form of therapy, liquid diet, and how many showed an increase in body fluid, as a result.

There is no doubt that this is a thought provoking paper and it would be both interesting and instructive to have the further views of the authors as well as any evidence for the controversial points they have raised.

Thank you very much.

Yours very sincerely,

RICHARD X. SANDS, M.D., F.A.C.O.G., F.R.C.O.G. Woman's Hospital, New York City

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### Boston Physicians Reply To Obstetrician's Comments

The Editor Southwestern Medicine

Dear Sir:

We wish to thank Dr. Sands for his fine letter, and we are quite flattered that he took such detailed interest in our paper.

At the onset please let us reiterate the primary point of the paper. It is that we were endeavouring to find a safe appetite depressant to be used in selected cases in our private obstetrical practice. We were not trying to make circus fat ladies thin, but rather attempting to keep the prenatal weight gain within the normally accepted limits.

We have long felt that various obstetrical catastrophes can be prevented by adequate prenatal nutrition; and, conversely, many complications of pregnancy are the result of nutritional deficiencies.

In the original paper we did not include our routine prenatal diet. Of course, it is tailored to the day-by-day requirements and individualized during stresses of physiological disturbances. Since the program was relatively long ranged, there was no abrupt restriction in the basic diet. The caloric intake is increased by trimesters from 2100 to 2500 to 3000 calories. Protein, both animal and vegetable, is within the range of 85 to 110 grams daily, especially in late pregnancy when the maternal organism will store over 100 grams daily in anticipation of labor and lactation. To enhance the utilization of vitamins and energy 80 to 100 grams of fats are included daily. The carbohydrate fraction may be varied to suit the caloric requirements especially in relation to excessive weight gain, and this measures 100 to 300 grams daily. This also gives added energy to the mother and is easily assimilable food for the fetus.

### Rapid Growth

During the 40 week span of pregnancy occurs the most rapid growth of life, for growth begins with conception and not with birth. This aggressive parasitism of the fetus soon exaggerates any pregavid nutritional deficiencies. It is well known that especially in the lower income families faulty nutritional habits are constant for generations. Then, too, in the U.S. the adolescent girl has the poorest diet of any member of the family. So, prenatal nutritional advice is invaluable and comes when a girl will most readily accept it, for the baby is the most important happening in her life.

As we stated in the paper, unfortunately the true appetite depressant drug which specifically reacts on the neural pathways to the hypothalmus has yet to be discovered; but dextro-amphetamine sulphate has inestimable value in controlling the desire for food and reducing the level of satiability to a normal one. Many, many papers have borne out the efficacy of this drug. As a matter of fact, we

counted 49 compounds listed in the "PHYSI-CIANS' DESK REFERENCE" that have made use of dextro-amphetamine sulphate in the preparation of an appetite control type drug. Thus the dextro-amphetamine sulphate results were used as a base line in our paper, and these results were closely paralleled by "AYDS."

### Control Group

Dr. Sands stated that our control group would have been more accurate if they were "untreated." We hope that he does not mean unadvised; for it is the responsibility of the private physician conducting the prenatal care to make an all-out effort to ensure the physical stamina of the mother and the constitutional adequacy of the newborn.

We disagree with his statement, "pregnancy is a diabetogenic state." Prediagnosis diabetes is well recognized as an important stage of the diabetic syndrome. Prediabetes is usually diagnosed from suspicion and past history. In our series there were no known diabetics, excessively large babies, or still births.

As for liquid diets, there are some that contain more than five grams of sodium which is far in excess. Because of the greater antidiuretic activity during pregnancy, fluid intake must be carefully controlled if there is a sodium imbalance and renal excretion promoted.

ELMORE M. CAMPBELL, M.D., Boston Visiting Obstetrician and Gynecologist, St. Elizabeth's Hospital, Boston, and St. Margaret's Hospital, Boston.

Andrew J. Gorman, M.D., Boston Senior Visiting Obstetrician and Gynecologist, St. Elizabeth's Hospital, Boston.

"It's easier to save money than it is to lose weight."

—James G. Taylor, M.D.

Nacogdoches, Texas

### Clinical Pathological Conference

R. E. Thomason General Hospital, El Paso

Case No. 1682, November 16, 1961

F. P. Bornstein, M.D., Editor

Presentation of Case By: Antonio Dow, M.D. History By: L. A. Gladstone, M.D.

The patient, a 61-year-old white male, was admitted to the hospital on 9/15/61 in a state of shock, promptly after he was shot with a .38 caliber revolver into the right upper abdominal quadrant. Except for right upper pulmonary lobectomy due to an abscess five years ago, he had apparently been in good health previously.

On admission the patient was unresponsive, blood pressure varying from 60/0 to 70/40. Pulse was not recorded. About 50 minutes after admission an exploratory laparotomy was performed. It was observed by the surgeon and stated in the operative record that the patient was in deep shock and paralysed from the waist down.

A preoperative portable film of the abdomen revealed a large metallic fragment lying in the "left lateral abdomen and a smaller one more medially". A portable film of the lower spine revealed a "small metallic fragment in the soft tissue of the back at the level of the L-3 and L-4 interspaces on the left". A portable chest film showed old bilateral apical scarring, slight elevation of left hemidiaphragm with suggestion of basilar atelectasis; otherwise no remarkable pathology was noted. CBC on admission showed a Hgb of 11.5 gms, hmcrt of 40 per cent, WBC of 21,800 with a moderate left shift.

During surgery 11 units of blood were administered rapidly. The abdominal cavity was entered through a midline incision extending from the xiphoid-sternal junction to below the umbilicus. Large amounts of clotted blood were noticed and removed. The liver was found to be uninjured. The stomach, spleen, duodenum, and the splenic flexure of the colon were found to be undamaged. A large hematoma was found to lie posterior to the duodenum.

Further exploration revealed that serious bleeding was coming from one branch of the right renal artery going to the inferior pole. To control this the renal artery and vein were divided and ligated and the kidney was removed. At the conclusion of surgery the patient's blood pressure stabilized at approximately 120/80.

On 9/16/61 the patient was conscious, complaining of pain in the abdomen and in the legs. His temperature ranged from 100 degrees to 101<sup>4</sup>. His blood pressure ranged from 110/70 to 98/60. Later in the day he became quite restless and began to be incoherent. His hgb was 14 gms and hmcrt 46 per cent. Also on the 16th the serum electrolytes were as follows: C0<sub>2</sub>36 meq/liter, C1 95, BUN 28.4, K 5.1, and Na 150 meq/liter. He received several Tetanus toxoid and antitoxin in-

jections, procaine penicillin 600,000 v.i.d. Vistaril for restlessness. Chloromycetin 200 mgm every six hours, 1500 cc of 5 per cent distilled water, and 2,000 cc of glucose saline. No progress note has been recorded until 9/20/61; however, the following observations were recorded by the nurses:

9/17/61: Blood pressure ranging from 108/56 to 94/50, pulse 100 to 108 "weak". Resp. 30. Wangenstein draining well. Wangenstein output 525 cc; catheter output 350 cc to a total of 875 cc, i.v. intake 5000 cc of Ringer's lactate distilled water and distilled saline. 60 meq of HCl was added to one of the bottles.

9/18/61: Blood pressure 110/60-70/36. Coffee ground material draining from the stomach tube. Condition generally poor, abdomen distended, rational and complaining of pain. Output not recorded, i.v. intake 3,500 cc mostly distilled saline containing Levophed. EKG showed changes compatible with myocardial ischemia.

9/19/61: "Appears to have hallucinations, confused, abusive, and nasty." Given Vistaril I.M. for restlessness. Blood pressure 110/60. Output 2,250 cc, intake 2,200 cc. A KUB film taken on this day showed "scattered metallic fragments present about the left and medial aspect of L-3 and a bullet fragment further to the left". "The bowels are within normal limits". Films of the lower spine reveal "that the bullet traversed through an area corresponding to the pars interarticularis of L-3". This would mean that there is very likely interference with the spinal cord at this level.

9/20/61: "Patient confused. Confusion appears to be similar to delirium tremens." Vistaril was given for restlessness.

9/21/61: Hgb 11.3, Hmcrt 36 per cent, blood pressure 90/40. Temperature up to 1026 rectally. WBC 18,600 with left shift (74 polys, 10 stabs, 5 lymphs, 9 monos) CO2 25 meq, C1 111 meq, BUN 44, K 4.4, Na 158 meq/liter. Abdomen not distended, but no peristaltic sounds are heard. Patient confused. Coffee ground material in gastric aspirate. Output 950?

9/23/61: Tracheotomy "for the purpose of bronchial toilet". Upper one third of the abdomen wound almost completely dehisced. Temperature 103<sup>8</sup> rectally, blood pressure 110/50. Intake

4,000, output 2,400 cc. Continued confusion and coffee ground material via the gastric tube.

9/26/61: Entire abdominal wall dehisced and abdominal organs have eviscerated. Under general anesthesia the peritoneal cavity was explored. An abscess in the subhepatic region was drained. The stomach and pylorus appeared normal. A stab wound was made to the right of a previous surgical incision. A drain was placed into the subhepatic area and the abdominal wall was closed with stainless steel wire sutures. Two units of blood were given.

9/30/61 -10/2/61: ACTH 20 mgm I.M. three times a day was begun on 9/30/61. Chest X-ray revealed scattered broncho pneumonia. Edema of lower extremities and right hand was noted on 10/1/61. Patient confused.

CO<sup>2</sup> on 10/2/61 15 meq/liter, C1 122, Na 152, K 4.3, BUN 48. Serum protein 5.1, Alb 2.7, Glob 2.4, Hgb 10.2, Hmcrt 31 per cent, WBC 28,300 with marked left shift. Twenty-four hour intake 3,760 and total output 1,680 cc. Chloromycetin was discontinued and started on Streptomycin gram I, I.M. and Achromycin 500 mgm in each i.v.

10/3/61: Wound again dehisced. Treated by strapping. Patient critical. Subcutaneous emphysema of chest wall, face, and neck. Frequent loose tarry stools. Five hundred cc of blood given.

10/6/61: Serum amylase 148 units, BUN 52 mgm per cent, Na 156, K 4.9, Blood pressure 96/48, pulse 110. Continued downhill course. Temperature 100°. Started on Colymycin yesterday. Foley output about 450 cc.

10/8/61: 500 cc of whole blood given. Increasing respiratory difficulty. 500 cc of dark bloody fluid obtained via the Levine tube. Gradually dropping blood pressure. Expired at 8:45 P.M.

### Clinical Discussion

Dr. Antonio Dow: It is quite evident from reading the protocol, and reading the chart, that the patient didn't do well right from the beginning.

He came in following a gunshot wound in the right upper abdomen. I talked to the operating surgeon about the case, and, apparently, it was a very urgent case; the type of a case you want to get into and get out fast. I am not casting any aspersion against the operating surgeon because I am sure he did as well as anybody could have done under the urgent circumstances. He went in there and corrected what was the obvious trouble and got out. Anybody would have done the same thing. But, there was something there that was missed, because this patient didn't do well. He didn't do as well as a nephrectomy should do ordinarily, even though it was a trans-abdominal nephrectomy.

There are some people that claim that peritonitis often follows a trans-abdominal nephrectomy of a severely traumatized kidney. Whether or not the right sub-hepatic abscess that was found at the time of second surgery was due to external contamination, or whether it was due to a contamination from one of the abdominal viscera remains to be seen.

It is disturbing that we don't have any history as to the patient's previous mental condition, or his alcoholic history. We find that two or three days post-operatively he became incoherent and very difficult to handle. This could be either a continuation of his previous condition, before he got shot, or it could denote delirium tremens, which I consider a very serious post-operative complication. I had a hemorrhoidectomy once that got a post-operative delirium tremens and the patient passed away. The patient received ACTH because of his mental state. I see no evidence on the chart that a culture was done and the x-rays ever really gave much help.

Doctor Stokdyk, would you at this time show us the X-rays. The X-rays were all portable X-rays and they are confusing and hazy. I really never could get anything diagnostic from them.

Dr. G. Stokdyk: As we know, the films were all taken supine. This is a frontal supine film of the chest so you can't even pick up any air under the diaphragm. This next is pre-operative chest film which was mentioned in the protocol; it shows nothing remarkable, except the scarring in the right upper lung field. I believe they mentioned the previous lobectomy in the protocol, which was

no doubt the cause of this pleural scarring.

On the pre-operative film of the abdomen we see a large metallic fragment on the left and smaller fragments from medially. In the post-operative film, dated the 19th we have a better visualization of the structures. We see that the left posterior neural arch of L-3 is destroyed, and we have a scattering of fine metallic fragments proceeding hence to the major portion of the fragment, the bullet proper. Here again we don't have any chance to see air under the diaphragm. You notice there is no air fluid level in the stomach, so we can immediately assume that this was not an upright film.

We also have to think about the coffee ground material in the Levine tube, and towards the end, about the tarry stools. Now, if he had been drinking before admission the blood could have been due to gastritis. We don't know whether he had a history of a duodenal or peptic ulcer. ACTH given towards the later post-operative period would, of course, aggravate the ulcer if present.

What else did the bullet do as it went from the right side anteriorly down to the subcutaneous region on the left side posteriorly?

All afternoon I was looking at cross-sections of the abdomen, at the various levels. At levels L-1, L-2, and L-3, the right colon always seems to hit me in the face. It is always lying right over that right kidney. It is rather hard for me to conceive how a bullet could have gone through and hit the pedicle of the kidney and escaped the right colon. I only mention that because I have nothing else to pick at. I think a colon perforation, especially of the ascending colon, in that area should be considered. You might say that the operating surgeon could have found it had it been there, but with all that blood in that area retroperitoneally and all the blood infiltrating into those adjacent tissues, I can conceive of how one could easily miss a lesion in that portion of the colon.

Furthermore, in the region of L-2 the duodenum turns around and joins the jenuum at the region of L-2 and L-3. There are some fragments of bullet in the region of L-2 and L-3 posteriorly, so that I wonder whether the duodenum would have been nicked by the bullet. On the other hand, reading the chart, I see no mention of bile drainage from

the wound. There was profuse purulent drainage after it was closed the second time, but never any bile drainage. The drainage was never characterized as foul.

These are films taken the 19th, and show the oblique views of the lumbar spine. We get a little better look, apparently, at the posterior neural arches, and these confirm the previous appearance of there being posterior neural arch damage. Apparently the posterior spinous processes are fairly intact, except for the third lumbar here. The intestinal pattern is never remarkable.

This next is a pretty fine film, giving an overall look at the lower spine here. We see definite evidence of diffuse calcification of the lower abdominal aorta without evidence of aneurysm.

Dr. Dow: So then we are left with the blood, the Levine tube, the tarry stools and the right subhepatic abscess, and the general poor post-operative response of the patient. The patient didn't do as well as he should have done, if the kidney had been the only trouble. I think that possibly there must have been another injury, probably to the large intestine, possibly also to the stomach and/or duodenum, although at the second operative procedure, the stomach and duodenum are described as normal.

But, we have got to explain the bleeding in the upper gastro-intestinal tract. We have got to explain the tarry stools. Now, we had no stools until close to the end. That means he had a very severe ileus. He must have had severe ileus to dehisce. So just guessing, I think this man has another lesion, probably in the colon, possibly in the stomach or duodenum. And, I think he had delirium tremens post-operatively. Maybe there is a bug there. He may have been confused before, in which case you have to consider other rare situations, which I don't think I will bring up. That is about all I can suggest. There must have been some other lesion, another perforation in the intestine that wasn't recognized.

Dr. D. Rathbun: Might I bring up the possibility that this man may have had a meningitis? This man obviously didn't do well. He didn't do as well as he should have, with the surgery that he had and with the care that he had. We have the note that he was paraplegic, but we don't have any

notes later on as to what his state of consciousness was, the last three or four days at least. He did receive transfusions and was in sort of a semi-shock level most of the time, and the last blood count that I saw reported was 28,000. He had a poor temperature response, 100 rectally, in spite of that extremely high white count with a marked shift to the left.

On the basis of the x-ray, one of those particles of the bullet must have gone through his spinal cord. We have no evidence to rule this out, since a spinal tap apparently was not done. If the paraplegia persisted, which apparently it did, and his course went downhill as markedly as it did, in spite of the care that he received, I presume that he was probably in a coma when he died. The only description that I saw was that he was critical each time.

We can certainly explain his poor course with a meningitis, if we assumed one of those particles went through his spinal cord, producing the paraplegia, he would almost very certainly have had a meningitis, because that particle must have contaminated his spinal cord. Because of his age he had a poor temperature response. Other than that I don't have any other comments.

Dr. E. S. Crossett: Except for the fact that the bullet went through his spinal cord what findings were present that would suggest a meningitis. So what could also be explained on the basis of a sympathetic abscess and the dehiscence of his wound, and the bleeding from his gastro-intestinal tract?

**Dr. Rathbun:** There wasn't anything specific other than that he was doing poorly all the way around. He did extremely poorly and nobody has explained why he did this. He may have well had multiple other injuries to his internal organs.

A Physician: Would the meningitis be responsible for his ileus and bleeding from the gastro-intestinal tract, and all of that?

Dr. Rathbun: No, I am not trying to explain all of these other findings on the basis of meningitis.

Dr. G. W. Iwen: On the 18th day after injury, that is the third, mention is made that subcutaneous emphysema of the chest and base of the neck

was present. Ten days previously he had a tracheotomy, and there was no mention made immediately afterwards that he did have subcutaneous emphysema. It is very possible that the subcutaneous emphysema arose from the perforation of the tracheotomy. The x-rays of the chest did not suggest a subcutaneous emphysema shortly after the tracheotomy. I was wondering whether this may have represented a gas from organisms that caused clostridial infection and that the subcutaneous abscess actually could have been a clostridial type of abscess, and that this air was not from tracheotomy but from infection.

Dr. Dow: I thought about that, because I have been sensitized to this clostridial infection by virtue of a recent case of mine, but the subcutaneous emphysema was limited to the neck and to the chest and not to the abdominal wound, and I asked the attending men specifically about that. There was no subcutaneous emphysema there. The only thing I could figure was this: That they didn't take good care of the tracheotomy opening and he blew some air subcutaneously. If the opening were clogged it would do that, If the wound is sutured tightly about the airway, it frequently will produce subcutaneous emphysema.

Dr. Van Waggoner: Doctor Dow, I can add one or two facts to this case. One is, after his death his brother told me that he had been an alcoholic for a good many years, quite a heavy drinker, which confirmed your suspicions probably.

Dr. Nathan Kleban: This man's albumin on Oct. 3 was 2.25, which is an indication that his state of protein nutrition was inadequate, and the time in the hospital was sufficient to explain that, so his protein nutrition was inadequate to start with.

Dr. Dow: With this additional history of chronic alcoholism we begin to understand the facts, because chronic alcoholics don't heal very well.

Dr. S. Heinemann: I would just like to point out, there was a paper written in 1939 or 1940, by one of the doctors in Memphis who got hold of a series of surgical cases from one of these Tennessee mountain sects who were vegetarians; and I think his experience was that about 20 per cent of this group dehisce. Then he finally got wise to the fact that the protein deficiency in patients did contribute to the dehiscence.

Dr. Saul Appel: Since we have been discussing

this as surgeons, I think the medical men ought to say something. Before we found out that he was an alcoholic, I would have suspected that he was a very heavy drinker, and had not been in good health for several reasons: One is he was shot. People that are shot usually are in an unhealthy environment. Two, he had a pulmonary infection five years previously which resulted in one abscess which had to be corrected surgically, and it is notorious that people in poor general health can more easily develop an abscess, especially an alcoholic who was sleeping one off, and may have aspirated something into his lungs and then developed an abscess; so that also substantiates the fact that he probably was a heavy drinker; and then there was the development of delirium tremens shortly after surgery, of course. One other thing that intrigues me about this case was the possibility also that this man may have had some renal damage, bilateral kidney disease before this surgery, and that by removing the right kidney we may have left the left kidney as the only one and, that one being in a diseased condition.

### Clinical Diagnosis

- 1. Bullet wound.
- 2. Post bullet wound infection.

Dr. Dow's Diagnosis: Abdominal bullet wound with probable perforation of the stomach or colon, possible post operative delirium tremens.

### Pathological Discussion

Dr. F. P. Bornstein: This was the body of a 61-year-old man measuring approximately 170 cm in length and weighing approximately 95 kg. Rigor mortis was nearly gone and there was moderate lividity of the dependent parts.

There was a fresh tracheotomy wound in the neck. There was a thoracotomy scar running across the right side of the thorax starting at the midline and running transversely for about 30 cm ending 15 cm below the right axilla. On the right side of the costal arch 13 cm to the right of the midline is an oval-shaped wound which measures 11 mm across. There is a recent surgical wound running downward from the xiphoid process in the midline for 20 cm. Located beneath the oval-shaped wound on the right costal arch was a transverse scar measuring three cm in greatest diameter di-

rectly below the oval-shaped wound. About three cm further down is a transverse wound of 2.5 cm with dirty rotten edges.

In evaluating the rest of the autopsy I would like to point out that there is nothing as difficult to evaluate as a bullet tract. This is especially true because we are usually thinking in systems like "the central nervous system," "the gastro-intestinal system," "the urogenital system". The bullet tract is no respecter of systems but goes through all kinds of systems in its course. Even a fresh bullet tract is hard to evaluate. If the patient survives for a time and there are surgical modifications this difficulty increases considerably.

To continue; having given you the approximate entry of the bullet next we turned the patient over and found the bullet in the left flank, 10 cm. to the left of the midline about the level of the third vertebra. The bullet measured 15 x 8 x 8 mm, was of soft lead with a flattened out nose.

The internal examination revealed a subacute peritonitis with free pus between the transverse colon and the gallbladder. There was a hole in the anterior wall of the stomach near the minor curvature and this perforation was covered with fibrin.

On entering the retro-peritoneal space a large hematoma was found in the region of the right psoas muscle with an abscess along the body of the third thoracic vertebra. There was a hole in the body of the third thoracic vertebra and obvious necrosis in this region. After part of the bones of the spinal column were removed obvious damage to the cauda equina was noticeable. Then in removing the central nervous system a fresh inflammatory membrane composed of purulent material was found in the space between the dura mater and the brain. Obviously then the infection of the third vertebra and the spinal canal had ended with an ascending inflammatory process inside the spinal canal.

# Anatomical Diagnosis

- 1. Bullet wound through abdomen with damage to intestinal tract and location of bullet beneath the skin.
- 2. Localized peritonitis.
- 3. Osteomyelitis of third lumbar vertebrae with ascending purulent meningitis.

Additional Comment: We have here a rather complicated chain of events starting with a bullet wound which produced intra-peritoneal perforation and shattering of the lumbar vertebrae. Recovery was obviously slow, and finally the damage to the third lumbar vertebrae produced an osteomyelitis and a secondary inflammatory process with pus extending along the spinal cord all the way up to the brain.

# Writing Contest Rules

Original scientific articles published in Southwestern Medicine will be eligible.

The contest for 1962 will close on Sept. 1, 1962, following publication of the August issue. Articles to be considered for publication in the August issue must be received by July 1, 1962. Articles not published with or before the August issue may still be eligible for publication and subsequent judging in the 1962-63 contest running from Sept. 1, 1962 to Sept. 1, 1963. Only papers acceptable to the board of editors of Southwestern Medicine will be published.

Awards will be made in two classifications: Regional and National. All physicians who practice in West Texas, Arizona, New Mexico, Nevada, or Northern Mexico (States of Sonora and Chihuahua) will be eligible to compete for the regional awards. All physicians in the

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Awards will be made in the following amounts:

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Contributions must be written in English, typed, double spaced on one side of paper only. A stamped, self-addressed envelope must accompany each paper to insure return of rejected manuscripts.

Papers should be submitted to Lester C. Feener, M.D., Editor, 310 North Stanton Street, El Paso, Texas.

# Coming Meetings

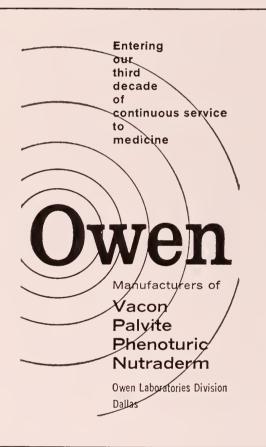
New Mexico Medical Society, annual meeting, Hobbs High School, Hobbs, N. M., May 8-11, 1962.

Texas Medical Association, Annual Meeting, Austin, May 12-15, 1962. C. Lincoln Williston, 1801 North Lamar Blvd., Executive Secretary.

New Mexico Chapter, American Academy of General Practice, Summer Clinic, Ruidoso, N. M., July 16-19, 1962. The Western Association of Railway Surgeons, annual meeting, Stockmen's Motor Hotel, Elko, Nev., Sept. 27-29, 1962.

Southwest Obstetrical and Gynecological Society, 12th Annual Meeting, Camelback Inn, Phoenix, Oct. 10-13, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.



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VOL. 43, NO. 6

June, 1962



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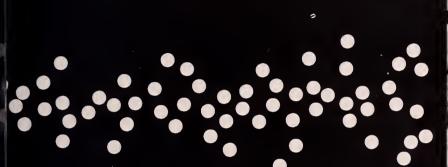
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\*Since the founding of Devereux Schools in 1912, a philosophy of Special Education and therapeutic techniques of rehabilitation and care have been developed for the sole reason of insuring to the greatest extent the future happiness and wellbeing of the retarded or emotionally disturbed child. Many of these techniques originated at Devereux Schools. This scries is launched during the Schools' 50th Anniversary in order that you may better understand the methods and goals of Devereux Schools.

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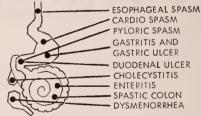
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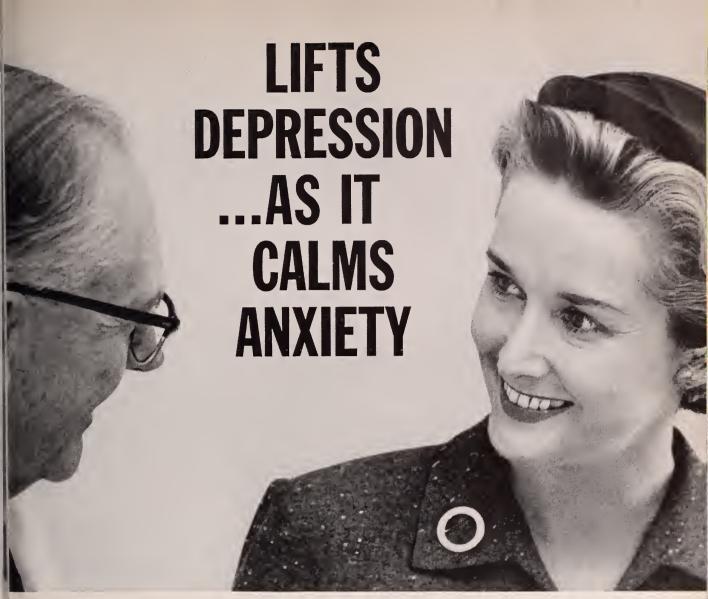
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VOL. 43

JUNE, 1962

NO. 6

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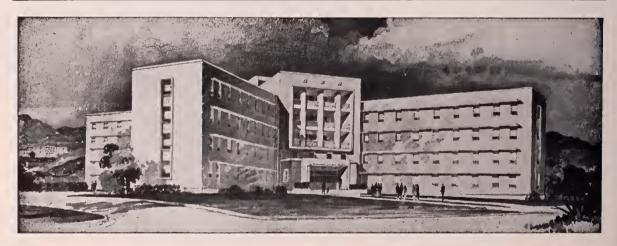
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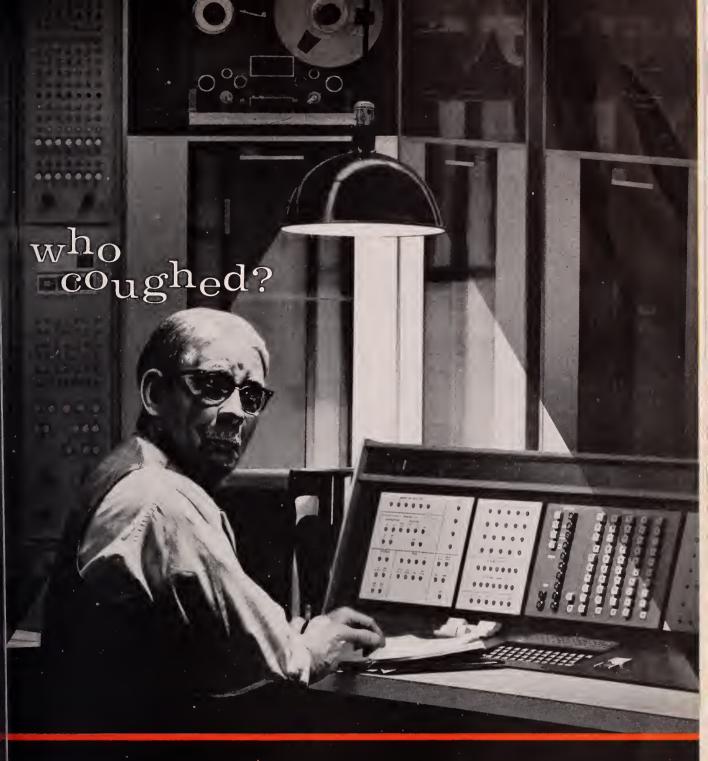
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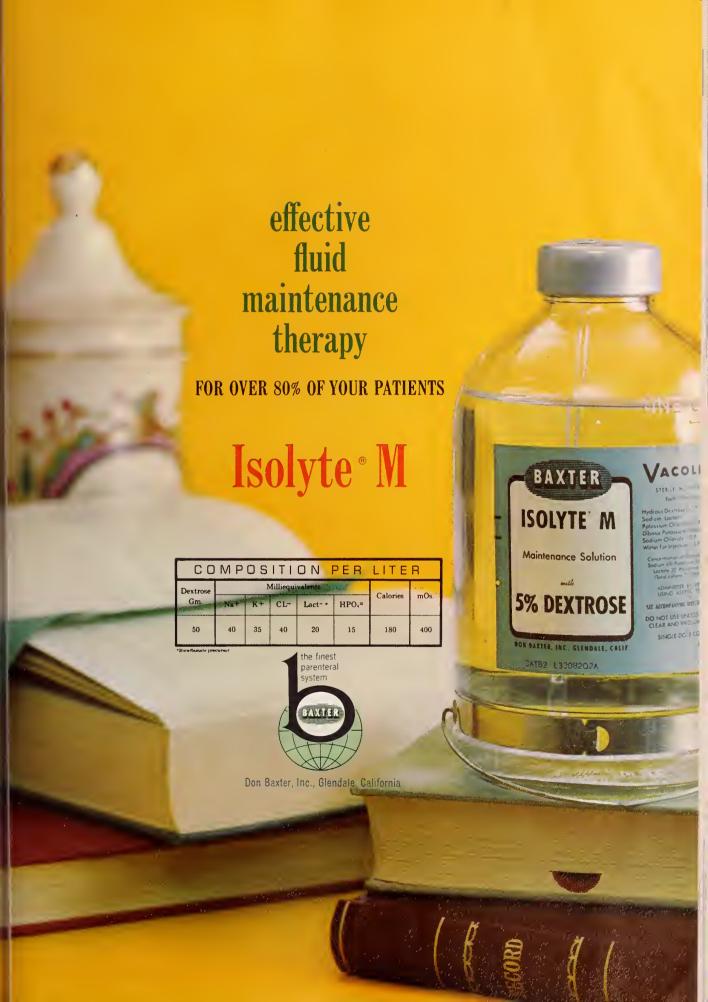


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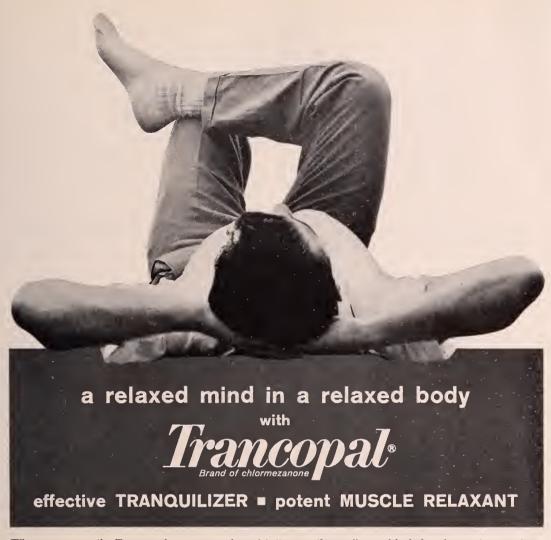






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References: 1. DeNyse, D. L.: M. Times 87:1512 (Nov.) 1959.
2. Gruenberg, F.: Current Therap. Res. 2:1 (Jan.) 1960.

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\*Maxwell, M.H., et al.: JAMA 170:917 (June 20) 1959.

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A A G P Summer Clinic in Ruidoso, N. M. July 16-19

The fifth annual Ruidoso Summer Clinic will be held high in the Sierra Blanca range at Ruidoso, N. M., from July 16 through 19, 1962.

The program will be presented by the University of Colorado School of Medicine. Speakers will be Dr. Gordon Meiklejohn, Dr. Colin H. Walker, Dr. C. Wesley Eisele, Dr. James S. Miles, Dr. Robert E. Dean, and Dr. Thomas E. Starzl.

Sponsored by the New Mexico Chapter of the American Academy of General Practice, the course earns a credit of 12 hours in Category 1 training.

Registrar is Dr. James A. Koch, 206 Dartmouth, N. E., Albuquerque, N. M., and housing requests should be directed to Dr. Bram Vanderstok, Box 116 in Ruidoso.

The clinic is being supported by a grant from Merck, Sharp & Dohme.

Dr. Jack D. Redman of Albuquerque is president of the New Mexico Chapter of the AAGP. Other officers are Dr. Frederick R. Brown, Ros-

well, president-elect; Dr. Walter J. Hopkins, Lovington, vice president; and Dr. James A. Koch, Albuquerque, secretary-treasurer.

The complete program is as follows:

# Monday, July 16

9:00-9:30 a.m. Respiratory Viral Diseases Gordon Meiklejohn, M.D.

9:30-10:00 a.m. Current Problems in Rheumatic Fever Diagnosis Colin H. Walker, M.D.

10:00-10:30 a.m. Poisons and Poisoners C. Wesley Eisele, M.D.

10:30-10:50 a.m. Intermission

10:50-11:20 a.m. Fungal Infections Gordon Meiklejohn, M. D.

11:20 a.m.-12:30 p.m. Question and Discussion Panel

# Tuesday, July 17

9:00- 9:30 a.m. The Role of the Practitioner in the Management of Congenital Heart Disease

Colin H. Walker, M.D.

9:30-10:00 a.m. Advances in Chemotherapy of Infections Gordon Meiklejohn, M.D. 10:00-10:30 a.m. The Internal Medical Audit C. Wesley Eisele, M.D.

10:30-10:50 a.m. Intermission

10:50-11:15 a.m. Office Interpretation of Heart Murmurs Colin H. Walker, M.D.

11:15-11:40 a.m. Medical Education and the Future of the General Practitioner

C. Wesley Eisele, M.D.

11:40 a.m.-12:30 p.m. Question and Discussion Panel

# Wednesday, July 18

9:00- 9:30 a.m. Problems in the Management of Duodenal Ulcer

Thomas E. Starzl, M.D.

9:30-10:00 a.m. Management of Positive Papanicolaou Smears During Pregnancy Robert E. Dean, M.D.

10:00-10:30 a.m. Indications for Operative Therapy of Fractures James S. Miles, M.D.

10:30-10:50 a.m. Intermission

10:50-11:15 a.m. The Current Treatment of Esophageal Diseases
Thomas E. Starzl, M.D.

11:15-11:40 a.m. Sepsis Associated with Ruptured Membranes Robert E. Dean, M.D.

11:40 a.m.-12:30 p.m. Question and Discussion Panel

# Thursday, July 19

9:00- 9:30 a.m. Benign Tumors of Bone James S. Miles, M.D.

9:30-10:00 a.m. Therapeutic Consideration in Breast Cancer Thomas E. Starzl, M.D.

10:00-10:30 a.m. New Thoughts and Practices in Obstetrics and Gynecology Robert E. Dean, M.D.

10:30-10:50 a.m. Intermission

10:50-11:20 a.m. Roentgenographic Determination of Lesions of Bone
James S. Miles, M.D.

11:20 a.m.-12:30 p.m. Question and Discussion Panel

# American Geriatrics Society to Meet in June

The 19th annual meeting of the American Geriatrics Society will be held June 18-20 in Chicago, with headquarters in the Palmer House.

A special session for laymen, "Partnership for Progress in Geriatrics" will open the two-day meeting. It will include discussions on The Importance of Understanding the Problems of Aging; Preparing the Mind for Maturity; and The Layman's Role in a Geriatrics Program.

Major areas for discussion will be geriatric medicine, geriatric surgery, geriatric cancer control, and geriatric socioeconomics.

All physicians are invited to attend. There is no charge for registration. Further information may be obtained from Mr. Henry Blanchard, Executive Director, American Geriatrics Society, 10 Columbus Circle, New York 19, N. Y.

# Management of Rectal Polyps

Edward S. Judd, M.D., Section of Surgery Mayo Clinic and Mayo Foundation Rochester, Minnesota

The following article was presented by Dr. Judd at St. Vincent's Hospital, Santa Fe, on April 24, 1962, preceding a Seminar on Surgical Lesions of the Colon, which will be published in an early issue of SOUTHWESTERN MEDICINE.

-The Editor

The importance of rectal polyps can no longer be denied. There has been much discussion concerning their relationship to cancer but argument on this point is beyond the scope of this presentation. Suffice it to say that my colleagues and I are convinced that cancer is an extremely important factor in any discussion of this type. Of less importance perhaps, but at times alarming, is the bleeding that may be seen with rectal polyps. On occasion this demands not only emergency treatment but vigorous replacement of blood by transfusion. A third feature is severe diarrhea which at times accompanies multiple polyps, especially those of the villous type. One of the more subtle aspects of the significance of rectal polyps is their function as sentinels. We have come to look upon the presence of a polyp in the rectum as a reminder that the colon not only may harbor other polyps at a higher level but also may be developing cancer in the near vicinity.

# Types of Polyps

The most common polyp is the so-called adenoma which, as its name implies, is simply a benign tumor of glandular epithelium. Microscopists may debate the presence or absence of malignancy within a given adenoma but ordinarily a truly benign lesion is rather well identified. These

polyps may be pedunculated, a factor that renders their treatment considerably easier and the prognosis better, or they may be sessile, a factor that renders treatment more difficult and causes more concern about recurrence and malignant transformation.

Malignant infiltration of a polyp introduces an entirely separate concern for the individual responsible for the patient's care. Obvious malignancy in the tip of a polyp that has a long benign pedicle is considerably less of a problem than is infiltration of a polyp that is sessile or possesses an extremely short pedicle. One's philosophy will vary with variation in the changes revealed.

A separate category is the actually malignant polyp that originates as such and is not a transformed adenoma. Then, too, a highly anaplastic malignant lesion may be discovered in the center of a large (otherwise benign) adenomatous polyp; the significant factor here is that one must obtain multiple specimens from such a lesion before one draws any conclusion. Not to be confused with this is a frank carcinoma that happens to be on a pedicle. The fact that it appears grossly to be a pedunculated lesion should not lull the examining

ORIGINAL ARTICLES

physician into a feeling of security, as this is a cancer and must be treated as such.

The "villous adenoma" is a peculiar lesion which, as the name implies, is a polypoid structure that may appear quite innocent histologically. However, its villous character causes it to extend over a large area in the rectum if treatment is delayed. The diarrhea accompanying a large tumor of this type can be not only annoying but also extremely incapacitating, owing to loss of vital serum electrolytes, especially potassium.

# Tendency on the Part of Polyps

On occasion polyps may be known to have been present for years and the patient known to have refused treatment or to have been unable to submit to treatment for various reasons. Some of these lesions appear to remain exactly the same over a protracted period. Others, however, change gradually into invasive carcinomas that finally demand an extremely radical operation. Prophylactic surgical treatment at an early stage in this situation has an obviously important part.

Another tendency that polyps exhibit is a peculiar propensity for developing in a multiple fashion. We are much more concerned about not only the rectum but also the remainder of the colon in a patient who has an assortment of polyps visible in the rectum. This always signifies to us that the possibility of colonic polyps is a real one. It also means that, although we are successful in our initial treatment of multiple polyps in the rectum, we must insist that the patient return for proctoscopic examination at stated intervals for the rest of his life.

# Diagnosis

At times the alert examiner will detect a rectal polyp or polyps on a thorough digital examination. More commonly the proctoscopic investigation is the key to the problem; the importance of this step in the physical examination cannot be overemphasized. X-ray examination of the colon has numerous shortcomings in this regard.

Although air contrast studies are most helpful in detecting polyps at higher levels, the roentgenogram may be practically useless in examining the rectum and rectosigmoid. This is a blind spot for the roentgenologist, and unfortunately patients are given a false sense of security if both the digital examination and the x-ray examination do not disclose any abnormality.

In our opinion it is mandatory to obtain a good proctoscopic examination before any final opinion is rendered. The best plan, we believe, is to perform the proctoscopic examination after the digital examination. If any polyps are disclosed in the rectum or rectosigmoid we proceed with x-ray examination to investigate the proximal reaches of the large intestine.

# Differential Diagnosis

A peculiar complication seen especially in ulcerative colitis is the formation of pseudopolyps. These may feel quite polypoid to the examining finger but on proctoscopic examination and biopsy they are seen to be mere tags of inflammatory mucosa and there are no adenomas or true tumor formation at all. At higher levels it may be very difficult to distinguish between pseudopolyps and true polyps, and on occasion surgical intervention will be the only solution.

Perhaps not completely germane to the present discussion is the condition known as multiple familial polyposis. Fortunately this is not a common condition but it is a striking one when seen. The important factor is that all of these patients die eventually of cancer of the colon if they are not treated early and well.

Usually the mere fact that overwhelming numbers of polyps are seen through the proctoscope suffices to make the diagnosis readily. A variant in the form of disseminated polyposis is seen; in this, the polyps are considerably less numerous but may give rise to some confusion. The combination of proctoscopic and x-ray examinations usually clarifies this quite well.

## Treatment

Fulguration has long been the treatment most readily available to the proctologist and certainly it has won its rightful place. Even if numerous polyps are present in the rectum, fulguration may serve to control the condition completely although numerous treatments may be required to clear the rectum of all polyps. When the polyp is on the posterior wall toward the center of the rectum, fulguration can be extremely thorough as there is no great concern about surrounding structures.

However, on the anterior wall of the rectum, where there would be possible complications in regard to the prostate gland, seminal vesicles, urinary bladder or other pelvic organs, deep fulguration is contraindicated. When the polyp is situated high in the rectum or in the rectosigmoid at a level where it might actually be above the pelvic fold of peritoneum, thorough fulguration is out of the question, as perforation of the bowel would result in contamination of the peritoneal cavity.

Before a polyp is fulgurated the proctologist must know its true nature, and this calls for biopsy. In actual practice the proctologist commonly fulgurates numerous polyps that have not been subjected to biopsy, because he can assume that many of these represent benign adenomas or that if a few malignant cells reside in the tip of the polyp his thorough fulguration is probably going to be good treatment anyway. If he knows some malignant cells are present he will need to fulgurate the normal-looking mucosa surrounding the polyp also, and this at times leads to complications.

In certain suspicious polyps it would appear to be good therapy to proceed with fulguration and apply radium to the surrounding area immediately afterward. We have no quarrel with this practice if the lesion is small and if it appears it can be controlled completely, since the only alternative, if the lesion is low in the rectum, would be complete sacrifice of the entire rectum and its sphincters.

In very elderly patients and in other patients for whom the surgical risk might be considerably increased because of general medical conditions, we do not hesitate to employ fulguration and to follow this with radium therapy. In fact, I am sure we have all accepted the risk even in lesions that are located rather high and have proceeded with fulguration, knowing that resection with anastomosis might be attended by a prohibitive risk.

In those cases in which malignant cells have been demonstrated in a polyp and in which the proctologist has decided upon fulguration as his treatment, he is always faced with concern regarding the lymph nodes, as they remain completely hidden. Ordinarily a low-grade inalignancy of polypoid nature is not accompanied by mesenteric lymphatic invasion, but on rare occasions we have all seen just such examples.

Our choice of treatment is not the decision of one person alone but a joint concern of the examining physician, the experienced proctologist and the surgeon who deals with lesions of this region. If at the conclusion of such a joint interview fulguration is elected, all three individuals make certain that the patient returns frequently for follow-up study.

Resection of the rectum becomes necessary in a certain percentage of these patients. If the lesion is definitely malignant, even though it is small and apparently possessed of a certain amount of pedicle formation, we have argued in favor of resection, especially if the anus and its sphincters may be preserved. Commonly in such a situation we perform low anterior resection, preserving the entire lower part of the rectum with the undisturbed anus.

Usually we employ an end-to-end anastomosis, and with modern methods of preparation and postoperative care the operative risk and morbidity rate may be kept at an acceptable level. Occasionally the lesion will be at a low-enough level that low anterior resection is extremely difficult or actually impossible. In such a situation a "pull-through" operation, perhaps preserving the entire anal canal intact, is preferable.

On certain occasions, however, even though a polypoid lesion of the rectum may seem small, if invasive malignancy is present and the lesion is too low for preservation of the anus and its sphincters we have not hesitated to proceed with radical combined abdominoperineal resection. Careful examination of the mesenteric lymph nodes in these patients will disclose occasional instances of involvement at some distance from the growth.

# Importance of Follow-up Examination

If there has been a single pedunculated polyp, especially of the benign adenomatous variety, there is no urgency about follow-up examinations and perhaps an annual physical examination to include proctoscopic investigation will suffice. It is not at all unusual for new polyps to be found; these

can be fulgurated easily, preventing what may have been a very serious lesion had it not been detected in this routine way. If we continue to look upon the single polyp as a sentinel of other possibly serious trouble we arrange the examinations at proper intervals and include x-ray examination of the colon, so that other lesions harbored at much higher levels can be detected in their incipiency.

In regard to disseminated polyposis in which perhaps six or eight polyps are scattered all the way from the rectum back to the cecum we are now finding a much more positive attitude throughout the surgical profession. Where repeated local excisions of polyps were formerly carried out, colectomy and ileoproctostomy are now performed. The rectal segment can then be kept under good control by periodic proctoscopic checkups. This eliminates the need for repeated abdominal operations and, far more important, it rids the patient of a potentially lethal colon.

In multiple polyps of the familial variety, followup examination is vital. If no malignant lesion has been disclosed in the rectum we have been in the habit of removing the abdominal colon and doing an end-to-end ileoproctostomy. The rectal segment can then be brought under control by repeated proctoscopic fulgurations until finally the rectum is entirely free. We make it a rigid rule that these people return at least once a year for the rest of their lives, as other polyps may well develop and these may be handled easily if they are disclosed in time. If they are neglected we are certain that cancer of the rectum will follow.

## Conclusion

There is no longer any argument about the importance of rectal polyps. Diagnosis is relatively easy and differential diagnosis poses no great problem. Where there might be some difference of opinion as to "shades of malignancy" or lethal characteristics of a given polyp, most authorities are agreed that vigorous treatment is demanded. When polyps are disclosed in time, they may be handled readily by fulguration, with radium occasionally being applied to the area. By close teamwork among internists, proctologists and surgeons the proper selection of patients for treatment by surgical resection, even by very radical operations when necessary, will produce gratifying results.

## Dr. Bate Named to AAGP Staff

Appointment of Thomas H. Bate, M.D., formerly of Phoenix, as director of the division of medical education on the administrative staff of the American Academy of General Practice has been announced by Mac F. Cahal, J.D., executive director of the organization, who said the new staff executive also will serve as secretary of the commission on education.

Dr. Bate's initial project will be to survey the status of general practice training at the medical undergraduate, graduate and postgraduate levels. In the area of graduate training, he will assist hospitals to establish two-year general practice training programs which meet approval standards of the education commission. He also will work

with medical school deans in developing general practice preceptorship programs at the undergraduate level. Amos N. Johnson, M.D., of Garland, N.C., is chairman of the commission,

Dr. Bate, 55, joined the Academy after two years on the staff of the American College of Surgeons, where he was a surveyor for the Joint Commission on Accreditation of Hospitals and an inspector for cancer programs.

He has been president, vice-president and a council member of the Arizona Medical Association; secretary of the Arizona Board of Medical Examiners; president of the Arizona chapter of the American Cancer Society, and a trustee of the Southwest Blood Banks, Inc.

# External Version in Breech Presentation\*

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Breech presentation and delivery must be considered abnormal obstetrical conditions. Several facts make this true. Cephalic presentation and delivery are more common, about 96 to four; they are safer by a factor of at least two or three times; and more complications relating to the infant occur when the obstetrical presentation is breech.

In certain respects breech presentation is similar to two other abnormal types of presentation, that is, the transverse and the oblique. Many points relative to breech are true regarding transverse and oblique presentations. In addition we can add that vaginal delivery of a term living infant from either of these two latter presentations is not possible. In our consideration of management of breech presentation it is in order to include that of transverse and oblique lies, because in some particulars these three can be grouped together.

The practicing of the skills of obstetrical maneuvers and manipulations undoubtedly reached its heights before the days of the safe cesarean section operation. During the 1920's and 1930's one does not find advocates of routine use of section for delivery of primiparous mothers with breech presentation as one does now. There were, however, discussions in journals and textbooks of that and former periods regarding such matters relating to breech presentation as the proper method of conducting the labor, the exact maneuvers in delivering the buttocks, shoulders, and head of

the baby, and also the questions of whether to turn the baby in utero from breech to vertex presentation.

The questions relating to external version were: How much risk is there of stimulating onset of premature labor? How many babies will turn themselves? How many babies will turn back to the original presentation after version? Does the incidence of abruption of the placenta increase? What is the danger of knotting the cord Rupturing the membranes? Ending up with a more unfavorable presentation than breech? What effect will external version have in the case of the three major conditions which cause the baby to occupy breech in the first place, i.e., contracted inlet, placenta previa, and hydrocephalus? Last and least, do more converted babies rotate to occipito-posterior than vertex babies?

## Method and Material

Consecutive obstetrical prenatal patients seen in private consultation compose the group from which breech presentation was diagnosed and external version done. Antenatal examination was done on the first office visit and abdominal palpation of the fetus in utero was carried out at each visit on and after the 30th week of gestation. It should be noted that in many cases the diagnosis of presentation of the baby could not be firmly established at the 30th week, but in nearly all instances it could be determined by the 32nd week.

<sup>\*</sup>Presented at Southwestern Medical Association annual meeting, Las Vegas, Nev., Oct. 19, 1961.

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In a few patients resort was made to AP and lateral x-ray views of the abdomen to confirm the clinical impression of the fetal position, but this was necessary fewer than five per cent of the times. Mostly, x-ray was asked for when twins or congenital abnormality of the baby was suspected.

As soon as breech presentation was discovered external version was attempted. The procedure consisted of, first, dislodging the breech from the pelvic inlet and then by even pressure on head and rump turning the baby in a forward somersault the necessary amount to bring the head over the pelvic strait. Proceeding slowly and pressing only during periods when the uterus was relaxed the manipulation took five to thirty minutes.

## Observations

Table I lists the number of times when breech and transverse presentations were found among 1409 consecutive antenatal pregnancy examinations.

## Table I

Incidence of breech and transverse, third trimester

Cephalic presentation	1214
Breech presentation	152
Transverse lie of fetus	43
Total	.1409

Since the occurrence of transverse lie in patients in labor is less than one in 100, most of these babies in the transverse could be expected to assume the longitudinal position and of those the majority would become breech. This combined number represents about 14 per cent. Average occurrence of breech and transverse presentation together at term in the parturient is close to five per cent. Thus, one has to do versions on two and one-half patients from the 30th week of gestation on in order to correct one breech in labor.

Or, stating it another way, of every 14 versions done in the third trimester seven would have been unnecessary as the turn would have occured spontaneously. There is, however, no way of telling which patients will have persistent breech and which will have spontaneous resolution before the event, so that it is necessary to convert all such

abnormalities found in the course of application of this maneuver. In tests and comparisons to determine the net value of external version due allowance must be made for the above demonstrated duplication of artificial and natural effort.

Detrimental effects of doing external version on 195 patients having breech presentation must be weighed against those in only 70 breech births, the anticipated incidence of breech deliveries and transverse presentation in 1409 gravid women.

How many of these abnormal presentations could be corrected by external version? Table II shows the results of application of this manipulation.

# Table II

Results of External Version	
Converted at first attempt	.124
Converted after more than one attempt	53
Converted prenatally, reverted to breech	
in labor	4
Unable to convert after repeated attempts	13
Vertex rotated to breech for first time	
in labor	1
Total	195

The successful versions are represented by the first two categories. The net result is 177 successes out of 195 attempts. For one reason or another, 18 patients were delivered as breech. Recalling our earlier calculation of some 70 expected instances of breech delivery in this group of patients we could state that the net gain was the averting of some 52 breech births. However, it should be pointed out that additional gain accrued from these conversions.

There was a disproportionately high incidence of obstetrical complications, and the management of most of these was greatly facilitated by having a vertex instead of a breech presentation. It should be noted that the majority of failures in normal patients having normal living babies occurred in primigravid women. Among the 13 women upon whom version could not be carried out there were 10 primigravid and three multigravid mothers. This finding is expected and is no doubt due to the presence of greater muscular tone in primigravidas.

The greater proportion of abnormal deliveries

in these 195 patients substantiates the fact that breech presentation is frequently complicated by coexisting abnormalities. A distinction should be made between breech presentation which is the sole abnormality of the gestation on the one hand, and breech caused or accompanied by other major obstetrical complication on the other. Table III displays the type of termination of pregnancies in which version was applied.

## Table III

# Type of Delivery

Vertex (vaginal route)	
Occipitoanterior	88
Occipitoposterior	8
Unknown	74
	170
Breech (vaginal route)	14
Cesarean section	11
Total	195

The occipitoanterior deliveries here can be considered as clear profit. The occipitoposteriors are not so clearly so, but one would rather have a posterior to deal with than a breech delivery. The 14 instances of vaginal breech delivery represent the failures of external version. In these patients there were no other contraindications to vaginal delivery. This does not mean that there were no complicating factors present, however. For example, one baby delivered vaginally from breech position was hydrocephalic.

The rate of cesarean section, six per cent, is higher than the 2.8 per cent rate among all 1409 patients. One primigravid patient was delivered by section electively after version failed. The indication was cephalopelvic disproportion.

Table IV details the reasons for cesarean section. As can be seen this group of patients was loaded with other obstetrical complications besides breech presentation.

Placenta previa is frequently associated with breech or transverse presentation of the fetus in utero. An obvious explanation is that the placenta, occupying the lower part of the uterine cavity, displaces the fetal head and even sometimes the

# Table IV

Sections in 195 Patients Initially Breech

Sections in 155 I defents Initially Diecen	
Baby delivered as breech at section:	
Cephalopelvic disproportion	1
Transverse lie	2
Prolapsed cord	1
Previous section	1
Baby delivered as vertex at section:	
Placenta previa	3
Abruptio placentae	1
Preeclampsia	1
Disproportion (hydrocephalus)	1
	_
Total	11

fetal presenting part whatever it may be. If one performs a version and finds that the head cannot be led into the pelvis but instead bounces around above the inlet, one should suspect placenta previa. One other instance of placenta previa was encountered in this group. This patient was delivered vaginally after external version prenatally and rupture of membranes at time of antepartal hemorrhage. The baby survived undamaged.

Proportionately more obstetrical complications occurred among these spatients than in consecutive prenatal patients. Table  $V_{\rm c}$  sets forth these complications.

## Table V

# Major Obstetrical Complications Among 195PatientsPreeclamptic toxemia5Placenta previa4Hydrocephalus3Abruptio placentae2Cephalopelvic disproportion2Prolapsed cord1Eclampsia1Perineal hematoma, postpartal1Total19

Congenital abnormalities of the baby, at least those of the neural system, are concentrated in babies presenting by breech probably because of mechanical factors. Three of the 195 babies were afflicted with hydrocephalus. Two were converted to vertex prenatally and one of these was delivered by section after a long trial of labor failed to produce engagement.

The other was delivered vaginally by tough midforceps when hydrocephalus was diagnosed during labor. The third hydrocephalic baby could not be converted and the mother was allowed to commence labor spontaneously with the breech presentation. Craniotomy on the aftercoming head completed this delivery. In hindsight, this latter outcome was to be preferred over that of the other two cases.

Separation of the normally implanted placenta occurred twice. In neither instance was it thought to be associated with the conversion of the breech antenatally. The separation occurred five and two weeks after the versions. In the former instance the bleeding was severe enough to require immediate section, while in the latter rupture of membranes and vaginal delivery was carried out.

The only instance of prolapsed umbilical cord came about because of the existence of a double footling breech. Version was tried on several occasions antenatally but could not be accomplished. When labor commenced spontaneously and membranes ruptured at 4 cm. cervical dilation, a long loop of umbilical cord was washed out through the vagina. Immediate section was resorted to but fetal circulation had been compromised and late mental retardation resulted even though the baby survived delivery.

Perineal hematoma, a troublesome complication, occurred but once. In this instance it followed vertex delivery after prenatal version of a breech. Thus, it was not related to breech delivery. Theoretically, at least, there might be a greater hazard of hematoma if one performed larger episiotomics for delivery of breech babies, this generally being the rule.

Aside from the additional scars on the myometria of the mothers due to sections, the real payoff in versions versus breech delivery is comparison of morbidity and mortality rates. Of the two seriously damaged babies one was mentally retarded due to anoxia incident to prolapse of the cord and one was hydrocephalic (still living at three years). Table VI lists causes of death in five infants dying during or immediately after delivery.

The uncorrected fetal mortality of two and one-half per cent is no more, no less than the average fetal mortality among all births in these consecutive patients. It is far better than the rate

# Table VI

# Mortality

Hydrocephalus	2
Hyaline membrane disease	2
Cephalopelvic disproportion, uterine	
inertia and prolonged labor	1

expected in breech delivery. Several examples from recent medical literature will illustrate. Jackson<sup>2</sup> reported 189 pregnancies in primigravidas with breech delivery, and associated with 11 per cent corrected mortality. Causes of death in the 20 babies which died were intracranial hemorrhage (7), pneumonia from amnionitis after premature rupture of membranes (5), atelectasis and generalized congestion (3), and remainder unknown. Twenty-two per cent of the babies were premature.

Sabin and Foote<sup>3</sup> studied breech presentation in the primigravida at Montreal and noted an uncorrected mortality of 12 per cent. Causes of death among these babies were similar to those of Jackson. Hall and Kohl<sup>4</sup> found a gross mortality of 14.4 per cent among their 1,456 cases. Dieckmann and Harrod<sup>5</sup> reviewed 1,061 breech deliveries having 9.8 per cent overall mortality rate. Appropriate allowance should be made for the fact that these patients were ward cases.

It is thus clear that when one takes a statistical look at the instances of breech presentation managed by external version and those allowed to progress to spontaneous onset of labor<sup>6</sup> with concomitant obstetrical care, the odds favor the former method of management.

# Summary

From this analysis it may be concluded that external version of babies in the transverse presentations is feasible and practical. The maneuver is accompanied by little danger. The earlier the version is attempted the easier it is completed; but also, the earlier the patients are examined the more frequent the finding of these abnormal presentations.

Version can be accomplished upon most babies in breech position and most of those successfully turned will be delivered as vertex. Occipitoposterior position appears to follow version with no more frequency than the random occurrence.

The coexistence of other major obstetrical complication does not necessarily contraindicate external version. Labor in the gravida with a borderline pelvis can be managed better with the fetus presenting by vertex. Marginal previa and low implantation of the placenta are better diagnosed and managed with vertex than with breech positions. It could be stated that when the fetus is found to have a large hydrocephalus delivery after craniotomy can be carried out better from a breech

than from a vertex presentation, but the choice in either case is not overwhelmingly favorable.

Contraindications to external version are clear from the nature of the conditions present: Labor, ruptured membranes, multiple pregnancy, antenatal bleeding, and large tumor of the uterus. Previous cesarean section might be added to this list in that it would be pointless to turn the fetus only to deliver it by repeat section. If one elected to deliver a patient with a previous section from below then external version would be beneficial.

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### **Hay Fever**

## Symptomatic Treatment With A New Anti-Allergic Compound

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This paper deals with the symptomatic relief of seasonal hay fever suffered by residents of central New Mexico during the summer months of 1961. A field-trial by 132 ambulatory patients was conducted with a multilayered tablet containing Chlorprophen pyridamine (Chlortrimeton (R), Teldrin (R) 12mg., Ephedrine, Sulfate ½ grain, and Atropine Sulfate 1/250 grain, produced at the suggestion of the author, and marketed as Histacon.\*

None of the patients had been on previous hyposensitization against pollens incriminated by routine intracutaneous skin testing and all were considered primary cases of seasonal pollinosis, on the basis of (1) history of annual seasonal recurrence, (2) demonstration of eosinophilia of nasal secretions by Hansel's Stain technique, and (3) immediate skin whealing by intracutaneous testing with aqueous extracts of pollen of plants in bloom concurrent with the patient's seasonal history.

Fifteen years ago the oral antihistamines first

<sup>\*</sup>Histacon, Marsh Emory Laboratories, Albuquerque

offered the hay fever victim relief from sneezing, itching of eyes and palate and profuse rhinorrhea; and gradually replaced the compounded combination of a sedative, a vaso constrictor (decongestant) of the ephederine type of sympathomimetic, and frequently an alkaloid of the atropine class for reducing excessive nasal secretions. The inclusion of the latter, in the opinion of the author, has been notoriously lacking in the many synergistic combinations of antihistamine-vaso-constrictor-sedative (or tranquilizer) compounds which have appeared during the past decade to reduce the side effects of the early antihistamines.

A high percentage of hay fever sufferers who are essentially ambulatory and seriously handicapped in their daily obligation, are indeed partially incapacitated for the seven months or more when pollens of hay fever-causing plants are continuously in the air in our Southwestern states. Side effects of the more potent antihistamines often preclude their daily use over such an extended interval.

### Histacon

Histacon was provided as a scored tablet, with a readily water soluble coating, beneath which the initial dose of the compound is available for rapid absorption. A pH sensitive layer prevents the release of the second dose of active ingredients incorporated in a hydrophilic resin (for more sustained action) until approximately five hours after ingestion. Since the highest pollen concentration of hay fever producing plants is in the air about dawn, most hay fever victims have their sleep disturbed about 5 A.M., to reach the most intense phase of hay fever during their preparation (including breakfast) for their day's work. Hence the importance of a delayed phase of a compound which can be taken orally on retiring.

### Methods

Manila coin envelopes containing approximately 20 tablets were issued to a series of ambulatory hay fever patients with written instruction to take one tablet at bedtime, the second after breakfast, and the third, if needed, mid-afternoon. Verbatim, telephonic, or in some cases, reports by mail were obtained from 132 patients as to (1) effectiveness in allaying symptons, and (2)

side reactions as either stimulation (i.e. insomnia), sedation or drowsiness, and excessive dryness of the nasal mucosa or mouth.

Efficacy was considered excellent in those cases preferring this compound to all other antihistamines or their compounds previously prescribed or purchased over-the-counter; as good, if equal in relief and duration of action; as fair if 50 per cent effective, but inferior to other products; and as poor if no change in symptoms was noted in one week.

It should be noted that none of the cases included were taking steroids, either orally or injectable, and that at the time of report, none had reached a level of hyposensitization by routine coseasonal methods of subcutaneous allergenic extract injections frequently started coincidental with completion of intracutaneous skin testing with pollen extracts. Cases of asthma, vasomotor rhinitis, rhinitis medicamentosa, and infectious paranasal sinusitis were not included in the survey.

### Results

Total Patients: 132

Results	No.	Per cent
Excellent		61
Good	24	18
Fair	17	13
Poor	11	8
Side Effects	4*	3

<sup>\*</sup>Dizziness; one reported gastro-intestinal cramping

### Discussion

While not a curative approach, the product in question would seem to offer satisfactory palliative relief to 79 per cent to 92 per cent of those hay fever victims of the Southwest who find their symptoms of such severity and length of season that they seek the services of allergic consultation and resultant hyposensitization. Symptomatic relief in the past years has run the gamut of topical nasal medications with vaso-constricting drugs, with or without antihistamines, usually irritating to the nasal mucosa because of a pH on the acid side.

Recently, the addition of topical steroids to intra-nasal sprays, suspension or solutions, has made these medications more acceptable to the patient

although conjunctival irritation, itching and lacrimation ordinarily require topical steroids as ophthalmic preparations for adjuvants. Their daily use over the five to seven months of hay fever symptoms experienced by victims in the Southwest is discouraged and in some cases disapproved by many practitioners. The third annoying symptom of palatal itching, often referred to the eustachian tubes is little reduced by topical applications.

It would appear that oral medication, if devoid of annoying side effects, and in such tablet form that the evening dose will allay matutinal symptoms, considered the peak of unpleasantry by most victims, would be most acceptable to the patient. Undoubtedly the steroids in adequate doses would offer as good if not better relief. However, the inherent dangers to the hypertensive, the diabetic, the peptic ulcer or the tubercular, should preclude their use over the extended weeks of our hay fever season. Other side effects of the steroids, such as weight gain, masculinizing effects on the female patient, and euphoria seen in many users of the steroids should mitigate against lengthy use in the ambulatory patient.

Migration to geographic areas in which the offending pollen is not found, for periods of five to six months, is not an economically feasible answer to many inhabitants of the area in which this survey was conducted.

Hyposensitization against offending pollens incriminated by skin testing is increasingly the answer to control, if not eventual arrest or cure of pollinosis. However, this takes time, and preferably foresight to realize the better results of preseasonal pollen therapy. The patient in the throes of hay fever takes a dim view of co-seasonal hyposensitization with its injections every two to three days, using highly dilute solutions of allergens productive of only fair relief, and almost always, in the author's experience, requiring adjuvant oral medication.

Self administered hyposensitization started during the hay fever season, with the patient already suffering from pollinosis is frequently attended by severe and dangerous constitutional or systemic reactions, often with wide-spread urticaria, laryngeal edema or frank bronchospastic asthma, to make the procedure dangerous and difficult to delegate by empirically scheduled dosages of antigens to a neighborhood nurse, or worse, in our rural ranching areas, to some member of the family who has the fortitude but little insight into the immensity and sudden onset of constitutional reactions.

### Conclusion

- 1. A new anti-allergic compound containing an antihistamine, ephedrine and atropine was distributed to 132 hay fever patients for symptomatic relief without, or prior to instigation of hyposensitization against pollens.
- 2. All patients had previously used oral antihistamines or vaso-constricting nasal preparations; none were on the steroids during the period evaluated.
- 3. Sixty-one per cent reported better symptomatic relief of hay fever than from antihistamines alone or in combination with tranquilizers or vasoconstricting drugs.
- 4. Seventy-nine per cent reported as good relief with Histacon; 92 per cent appreciable relief of symptoms.
- 5 Three per cent reported side reactions, as dizziness, sufficient to discontinue or reduce the dosage to such levels that it was not effective.
- 6. The compound, Histacon, is considered an excellent palliative compound for relief of seasonal hay fever in the Southwest.

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## Initial Treatment of Flexor Tendon Injuries of the Minor Fingers of the Hand

MORTON H. LEONARD, M.D., F.A.C.S., F.I.C.S., El Paso

The repair of flexor tendons in the fingers where they are encased in their dense fibrous tunnel constitutes a problem so severe that the level where the tunnel exists has been called "no man's land" by Sterling Bunnell. The difficulty stems from the poor blood supply to the tendons in these regions as well as from the presence of two tendons in a tight tube.

The flexor tendons in the palm receive nourishment from surrounding areolar tissue (paratenon). In the tunnel area their blood supply is derived but from the vinculae, the points of reflexion of synovial sheaths at their proximal and distal ends and from the insertions of the tendons.

The problem is compounded in this region extending from the distal palmar crease to just

beyond the insertion of the sublimii in the middle phalanx of the finger by the dense fibrous tunnel which constitutes a barrier to blood supply and cramps two tendons into a very small area. Repair of tendons in this area will more than likely result in adherence of one tendon to the other as well as to the surrounding dense fibrous sheath.

Because of the physiologic and anatomic facts outlined above the best course of treatment is suggested in the accompanying diagram.

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#### Reference

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1. Primary repair or tendon advencement.

One can sacrifice up to 1 inch of flexor profundus and not have a disabling flexion contracture.

Profundus only - Tenudesis of distal interphalangeal joint, Sublimis only - No repair, Sublimis and profundus - Careful cleansing and closure. Delayed tendon graft.

3. If laceration is located where
the sheath can be opened to permit sliding, remove sublimis
and repair profundus. (Injuries
sustained with finger in extensionTendon union can be made so that
the site of union will not be in
the tunnel.)

t. Sublimis only - No repair.

Sublimis and profundus - Primary
repair of profundus. Remove sublimis.

## Infectious Mononucleosis

M. R. CHAPPEL, M.D.

Director of Student Health
The University of Arizona, Tucson

Small doses of steroids were used for a short period of time to treat 111 cases of infectious mononucleosis. Early diagnosis and prompt treatment with steroids reduced the days of hospitalization and disability to a minimum and often eliminated hospitalization entirely. It was found to be a safe and effective form of therapy. There were no complications encountered by its use in 111 cases treated. It is the author's belief that steroids used early prevent the hepatosplenomegaly syndrome complications.

A diagnosis of infective mononucleosis in the past usually connotated a long period of disability. It has been found by the author and others<sup>1-9</sup> that this prolonged period of disability is preventable by the judicious use of small doses of steroids. It is the purpose of this report to present the results of studies in 111 cases using this form of treatment.

Previous to the use of steroid therapy in the treatment of infectious mononucleosis, the course of the disease usually ran from four to 12 weeks with bed rest a good part of the time. The majority of cases of infective mononucleosis occur in the student age group. Many students ill with infectious mononucleosis dropped out of school for a semester because of the prolonged period of asthenia. This problem is important because it represents a loss of time and money to the student, to his family and to his school.

Using the results learned from a double blind study done in 1956-579 as the basis of the treatment outlined below, the prolonged period of bed rest is seldom necessary. Early diagnosis and prompt treatment with steroids will reduce hospitalization and bed care to a minimum and often eliminate it entirely. An analysis of the statistics from treatment of 111 cases show that the disability from mononucleosis can be limited to a short period of time by the judicious use of steroids early in the disease.

During the last three years, the author has treated more than 111 cases of infectious mononucleosis with either Cortisone or Prednisone. The decision to use steroids was empirical, and the dose of steroids usually depended upon the amount of fever and asthenia present, and whether or not it was examination time at the university. At examination time students with in-

fectious mononucleosis were carried on steroid therapy throughout this period of extra stress even though their symptoms did not warrant it.

### Diagnosis Confirmed

The clinical diagnosis of infectious mononucleosis was confirmed in all cases by blood counts; particularly the differential blood count and a positive heterophile of 1:56 or greater. Those with a fever of 100°F. or above were put to bed until fever free. Steroids were started and when continued in adequate dosage, the patient usually became fever free in less than 12 hours. This striking fall in temperature occurred in those cases even with high fever.

Students without fever or fever below 100°F, were usually treated as outpatients and attended classes, but followed the same pattern of treatment as the more severely ill patients. Both bed and ambulatory patients with mononucleosis were usually started on Cortisone 50 mgm. T.I.D. orally.

The patients usually became symptom free in from three to five days, and then the dose of steroid was reduced to 25 mgm. Q.I.D. orally. If the patient continued to be symptom free and felt normal, the dosage was further reduced to 25 mgm. T.I.D. orally. In a few days the dosage was further reduced to 25 mgm. B.I.D. orally and when the patient continued to be symptom free, the steroids were stopped entirely.

Follow-up studies were made after three to four days without therapy, and if there was no recurrence of symptoms, no further treatment was given. If symptoms of asthenia, etc., persisted, one of the amphetamine compounds was given once a day after breakfast for three or four days for its euphoric effect. A recheck was made in seven to 10 days after medication had been discontinued, and if no symptoms were present, the patient was discharged as recovered. Hospitalized patients were seen every day and ambulatory patients every other day while on steroid therapy.

### Dosage Determined

In the cases reported, the only other form of treatment given was aspirin for fever above 100°F. and an antibiotic, usually oral penicillin, when the dosage of cortisone was above 100 mgm. per day. A high protein diet and one hour extra sleep per day were recommended. All contact

sports were forbidden for two months. The dosage of steroids was determined almost entirely upon how the patient felt; i.e. if he fatigued easily or if he lacked his normal energy, the steroids were continued. As soon as he felt normal they were discontinued.

In only two cases did the dose of 150 mgm. of steroids daily have to be reduced because of excessive euphoria. Both cases were female and acted euphoric and as though they were slightly inebriated. In both these cases this occurred after the second dose of 50 mgm. of cortisone orally and persisted for approximately two hours. It did not recur with a reduction in the following dose of cortisone.

One notes in the following statistics, that there is a discrepancy between the total cases reported with laboratory data and the total cases reported with clinical data; this discrepancy is accounted for by some of the patients lost in the follow-up after the laboratory work was done.

### Laboratory Data Total Cases: 117

Heterophile dilutions ranged from 1:56 to 1:7168. Highest lymphocyte count found: 89%. Average lymphocyte found: 66.46%.

Highest percentage of atypical lymphocytes: 80%.

## Clinical Data Total Cases: 111

Males 74; Females 37. This is the same ratio of males to females in the school population.

Six cases had frank jaundice and definite liver enlargement. All were jaundiced before treatment had been started. In three cases the spleen was palpated. All of these rapidly abated on steroid therapy.

No skin rash was seen in this series of cases.

Number of cases requiring bed care: 69.

Number of cases treated as outpatients only: 42.

Average number of days of bed care after diagnosis: 1.96 days

Average number of days of school missed after diagnosis: 2.1 days.

Longest time of treatment for any one case: 27 days.

Shortest time of treatment: 3 days.

Average number of days treated: 10.3 days.

Largest amount of steroid used in one case: 75 tablets or 183/4 gms.

Smallest amount of steroid used in one case: 8 tablets or 2 gms.

Average amount of steroid used per case: 32.2 tablets or 8 gms.

Number of students dropped from school on my recommendation: two; on outside physicians' recommendations: two. Total: four.

Number of cases who transferred to private physician's care: three.

Number of cases failing to return for follow-up after diagnosis: three.

### Complications of Treatment

Gastric distress occurred in two cases. These two cases continued steroid medication with the aid of alkalis and a reduction in the dose of steroids. Both remained symptom free when their final check up was made 10 to 17 days after therapy had been discontinued. No other complications were encountered that could be attributed to the therapy.

There were no patients in this series of cases who had a previous history of peptic ulcer or tuberculosis. Chest X-rays were negative on all at the beginning of the school year.

### Conclusions

- 1. The symptoms of mononucleosis can be controlled within a few days by the use of steroids.
- 2. Long periods of bed rest and disability can be eliminated by the use of steroids.
- 3. Students can attend classes and feel able to do so while under this type of treatment.
- 4. Liver function tests, sedimentation rates, blood chemistries, repeat heterophile, bilirubin tests, blood cultures, prothrombin tests, and other laboratory tests are unnecessary either to make a correct diagnosis of infectious mononucleosis or for follow-up studies for an adequate treatment of the disease. They add only to the expense of the illness.

- **5.** Steroid treatment of mononucleosis is safe; practically no complications occurred in 111 cases so treated.
- **6.** The early use of steroids in the treatment of infective mononucleosis probably prevents jaundice and hepato-splenomegaly syndrome.

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Southwest Obstetrical and Gynecological Society, 12th Annual Meeting, Camelback Inn, Phoenix, Oct. 10-13, 1962.

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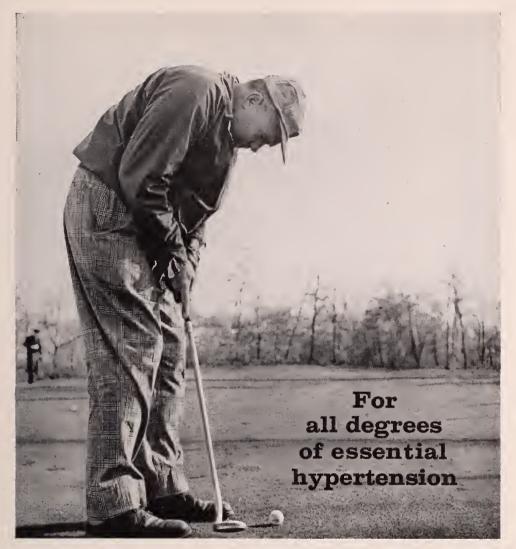
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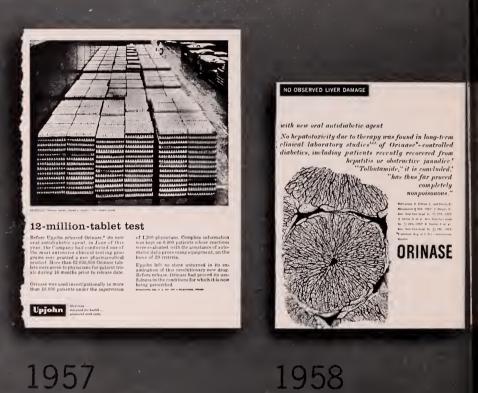
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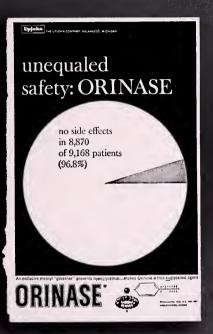
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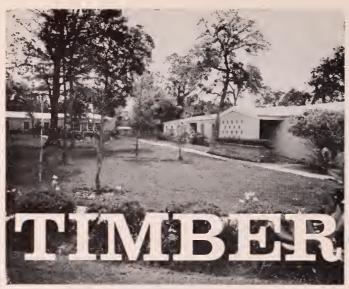
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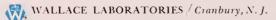
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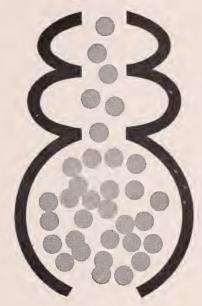
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- 1. Demeulenaere, L.: Action du R 1132 sur le transit gastraintestinal, Acta Gastraent. Belg. 27.674-680 (Sept.-Oct.) 1958.
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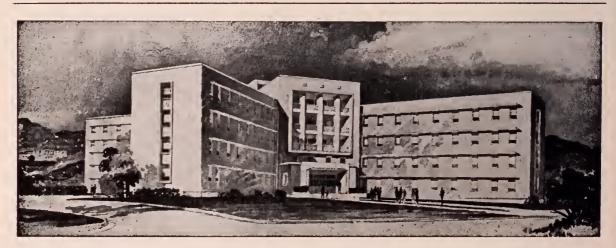
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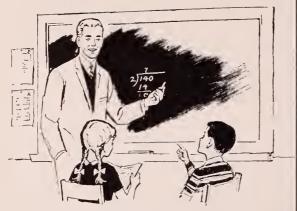


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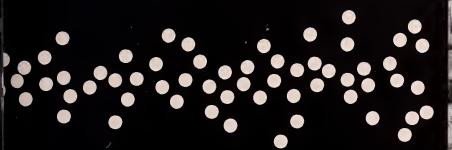
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SECOND ANNUAL NEW MEXICO A. H. ROBINS CO. AWARD—Dr. Roy F. Goddard, Albuquerque, second from left, receives the A. H. Robins Co. Award for Community Service at the annual meeting of the New Mexico Medical Society in Hobbs, N. M., May 8-11, from Dr. Everet H. Wood, Albuquerque, chairman of the state society's public relations committee. Others in the photo are, extreme left, Dr. William E. Badger, Hobbs, immediate past president, and right, Karl B. Eckhardt, Denver, representing the Robins firm. Dr. Goddard is director of the pediatrics research department at the Lovelace Foundation for Medical Education and Research in Albuquerque.

## Dr. Derbyshire Elected President Of

### New Mexico Medical Society

Dr. R. C. Derbyshire, Santa Fe, was elected president of the New Mexico Medical Society at its 80th annual meeting in Hobbs, N. M., May 8-11, 1962.

Other new officers are Dr. C. Pardue Bunch, Artesia, president-elect; Dr. T. L. Carr, Albuquerque, vice-president; Dr. Earl L. Malone, Roswell, delegate to the AMA; and Dr. Leland S. Evans, Las Cruces, alternate delegate to the AMA. Dr. Hugh B. Woodward, Albuquerque, and Dr. Omar Legant, Albuquerque, continue in their posts, respectively, as secretary-treasurer and speaker of the house of delegates.

The state society's 1963 meeting will be held in Albuquerque and the '64 session in Carlsbad.

Dr. Derbyshire was born in Hastings-on-Hud-





NEW OFFICERS—Shown with Dr. Leonard Larson, Bismarck, N. D., president of the AMA, front left, are new officers of the New Mexico Medical Society as follows: front row, left to right, Dr. R. C. Derbyshire, Santa Fe, president; Dr. C. Pardue Bunch, Artesia, president-elect; and, back row, left to right, Dr. Hugh B. Woodward, Albuquerque, who continues as secretary-treasurer; Dr. William E. Badger, Hobbs, immediate past president; Dr. T. L. Carr, Albuquerque, vice-president; and Dr. Earl L. Malone, Roswell, delegate to the AMA. Not shown are Dr. Omar Legant, Albuquerque, who continues as speaker of the house of delegates, and Dr. Leland S. Evans, Las Cruces, AMA alternate delegate.

son, N. Y.. and received his B.A. at Hamden-Sydney College in Hamden-Sydney, Va., and his M.D. at Johns-Hopkins University School of Medicine. He interned at Johns-Hopkins and then took a three and one-half year residency in surgery at the Mayo Clinic, He began the practice of medicine in Mount Airy, N. C., in 1941 and after 15 months moved to Albuquerque, where he practiced from 1942 until 1948. He was in Artesia from 1948 to 1950, when he moved to

Santa Fe, where he has since been engaged in the practice of surgery.

Dr. Derbyshire is certified by the American Board of Surgery and is a Fellow in the American College of Surgeons. He is also a Fellow in the Southwestern Surgical Congress, is secretary of the New Mexico Board of Medical Examiners and a member of the executive committee for the Federation of State Medical Boards of the U. S. and editor of its Bulletin.

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#### Mechanism of Blood Coagulation

ARMAND J. QUICK, M.D.

Department of Biochemistry

Marquette University School of Medicine, Milwaukee

The following article was presented by Dr. Quick at St. Vincent's Hospital, Santa Fe, on May 22, 1962, preceding a Seminar on the diagnosis and management of certain coagulation defects, which will appear in an early issue of SOUTHWESTERN MEDICINE.

-The Editor

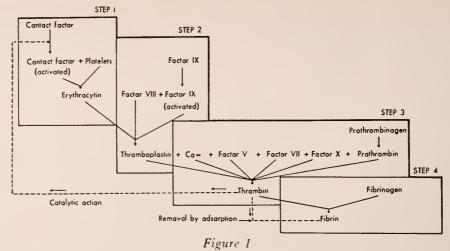
The interpretation of the coagulation mechanism in terms of physiological function is beset with serious difficulties. One must depend largely on data obtained under grossly unphysiological conditions. Blood is removed from its natural environment, subjected to rough foreign surfaces such as glass—totally unlike the endothelium—and tested with reagents which often have no resemblance to agents found in the body. But an even greater obstacle is the uncertainty regarding the physiological purpose of blood clotting.

The mechanistic concept that bleeding is controlled by a fibrin plug and that the clotting time is a measure of coagulability and of hemostasis is still widely accepted as a fact, whereas it is at best an unproved theory. Its validity is challenged by a number of cogent observations. In hereditary hypofibrinogenemia the bleeding tendency is strik-

ingly mild. Likewise, in a case of hyperheparinemia so pronounced that the blood is incoagulable, abnormal bleeding occurs only after severe trauma. Individuals with the Hageman trait may have a clotting time far longer than found in moderately severe hemophilia, yet are entirely normal hemostatically. A patient with thrombocytopenia, in marked contrast, may bleed profusely though the clotting time is hardly ever prolonged and sometimes even abnormally short.

Despite these complications, significant progress has been made in attaining a better understanding of the clotting reactions and in correlating this information with hemostasis. Many of the advances have come about through the development of quantitative tests for the various clotting factors. On the basis of results obtained from a few simple tests, it has been possible to construct a clotting scheme<sup>2</sup> (Fig. 1) which serves as a practical guide for the diagnosis of the bleeding diseases caused by abnormalities in coagulation.

Santa Fe Seminars are supported by a grant from the Merck Sharp & Dohme Postgraduate Program; and Dr. Quick's work was supported by a grant from the National Heart Institute, National Institutes of Health, U. S. Public Health Service.



A scheme to explain the coagulation of the blood. The autocatalysis is mediated through thrombin and the control by its adsorption to fibrin.

For convenience, the coagulation mechanism may be divided into four major steps, each one of which is sufficiently distinct to serve as a separate entity under which related defects may be grouped. Each step can be identified by one simple, single test. Because step four, which is the terminal stage, is the simplest and best understood, it is advantageous to reverse the order of sequence and discuss this last step first. To avoid making the presentation too complex, the diagnosis of only the more common and better understood bleeding diseases of each category will be considered. For the sake of conciseness, the detailed description of the various clotting tests will be omitted because they have been fully outlined previously.3

#### Step 4

#### Clotting of Fibrinogen by Fibrin

Characterizing test: Thrombin time Factors: fibrinogen heparin

The thrombin time<sup>4</sup> developed in 1936 which consists of adding a standardized amount of thrombin to a fixed volume of oxalated plasma is based on the principle that the clotting time of normal plasma under standardized conditions is proportional to the concentration of thrombin. Obviously, no clotting occurs when fibrinogen is below the detectable level. Hereditary afibrinogenemia, or more correctly hypofibrinogenemia because a trace of fibrinogen is usually found in the blood, is readily recognized by a total in-

coagulability. The diagnosis is confirmed by obtaining a normal thrombin time after mixing the plasma with an equal volume of normal oxalated plasma. With this simple procedure, inhibitors as the cause of incoagulability are excluded. (Table I)

Acquired afibrinogenemia is a fairly common condition encountered in obstetrical bleeding. It is probably brought about by a slow continuous leakage of thromboplastin or thrombin into the blood causing defibrinogenation. The loss of fibrinogen is accompanied by a decrease of other clotting factors such as factors V and VIII<sup>5</sup> which function in steps two and three.

Hyperheparinemia is an exceedingly rare disorder. It is probably hereditary since it has been observed in inbred minks. Despite the high concentration of heparin, which in one reported case rendered the blood incoagulable, the bleeding tendency has been amazingly mild. Secondary

Table I

Differentiation of Hyperheparinemia and Hypofibrinogenemia by the Thrombin Time

Hyperheparinen plasma Normal plasma		ml. 0.2	ml. 0.1 0.1		ml.
Hypofibrinogene plasma Thrombin			3.1	0.2	0.1
solution	0.1	0.1	0.1	0.1	0.1
Clotting time, sec.	7	180+	13.5		7

The heparinemic and hypofibrinogenemic plasmas were obtained from patients. The former contained approximately 10 micrograms / 1 ml. of blood.

hyperheparinemia, likewise, is uncommon and rarely causes serious bleeding. In animals, it can readily be produced experimentally with peptone or anaphylactic shock.<sup>6</sup>

#### Step 3 Conversion of Prothrombin to Thrombin

Characterizing test: One-stage prothrombin time

Factors: Prothrombin

Factor V (labile)

Factor VII (stable)

Factor X (Stuart-Prower)

The one-stage prothrombin time of normal adult plasma is remarkably constant, provided the test is carried out correctly. This constancy is due to the genetic fixation of the free prothrombin concentration. The free prothrombin constitutes 25 per cent of the total. The inactive portion, designated prothrombinogen, has no effect on the prothrombin time until activated. Two types of hereditary hypoprothrombinemia have been discovered:<sup>7,8</sup> Type I in which both the free and the total prothrombin are low, and Type II in which the free is low but the total prothrombin is normal. (Fig. 2)

The hereditary hypoprothrombinemias are the only known states in which the deficiency is solely that of prothrombin. In the acquired hypoprothrombinemias, other clotting factors are invariably found to be reduced. The one-stage prothrombin time becomes specific for prothrombin when it is found that neither the addition of factor V nor factors VII and X to the plasma brings about correction. (Table II) Quantitatively, prothrombin is an important factor in hemostasis. Even when reduced to only 30 per cent of normal, a frank bleeding tendency is manifested.<sup>8</sup>

Factor V has no influence on the prothrombin time of normal plasma because it is in excess, whereas free prothrombin is the limiting factor. A deficiency is readily recognized by a prolonged prothrombin time which is normalized to 12 seconds on the addition of excess factor V to the plasma. (Fig. 3) A deficiency solely of factor V is very rare and is found only in the hereditary disease. In a family recently studied, three siblings were found who have a prothrombin time of 50 seconds. This corresponds to a concentration of less than 5 per cent of normal, yet the bleeding in these children has been mild.

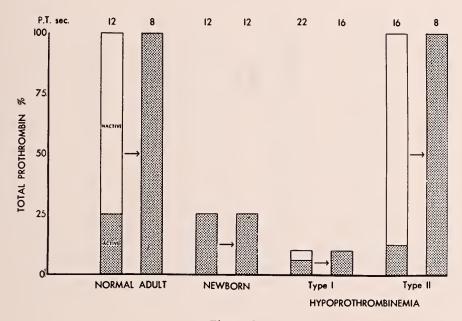


Figure 2

The active prothrombin, which is the same in the newborn as in the adult, determines the one-stage prothrombin time. Newborn plasma lacks reserve inactive prothrombin which in the adult constitutes 75 per cent of the total. In Type I hereditary hypoprothrombinemia both free and total prothrombin are low, whereas in Type II, the free is diminished and the total is normal.

Acquired factor V deficiency is always accompanied by a decrease of other clotting factors. At the time of the discovery of this factor, <sup>10</sup> it was noted that it can be decreased by experimental liver injury. It is also greatly decreased in experimental defibringenation produced by a slow continuous intravenous injection of thrombin.<sup>5</sup>

Factor VII deficiency is characterized by a prolonged prothrombin time which is corrected by the addition of aged serum to the plasma. It is to be noted that even in severe factor VII deficiency, the clotting time, the prothrombin consumption and the thromboplastin generation tests are

Table II

Differentiation of Hypoprothrombinemic States

		Prothron	ibin Lime
	Basic	With added factor V*	With added factors VII and X*
	sec	sec	sec
Normal	12	12	12
Prothrombin deficiency	70	60	55
Factor VII deficiency	60	50	12.5
Factor X deficiency	16	16	12
Factor V deficiency	55	12	51
www.iii. 1 1 1 1	1.1 (7)	(DO)	1 .1

\*Rabbit plasma absorbed with  $\text{Ca}_3(PO_4)_2$  was used as the source of factor V and aged serum as the source of factors VII and X

normal.<sup>11,12</sup> Only a few cases of hereditary factor VII deficiency have been reported. The severity depends on the level in the blood, as measured by the unmodified one-stage test which is highly sensitive to a deficiency of factor VII, provided a thromboplastin is employed such as rabbit brain which is not contaminated with serum.

The most important aspect of factor VII is that its production is dependent on vitamin K. When this vitamin is made unavailable either through a deficiency in the diet or by a vitamin K antagonist such as Dicumarol, the level of factor VII promptly begins to drop and this is followed by a proportional decrease of prothrombin. A definite ratio between the depression of factor VII and the prothrombin is found. (Fig. 4) It is quite probable that the antithrombotic action of Dicumarol depends basically on the depression of the prothrombin level and that the significance of factor VII lies in its effect on the production of prothrombin. A prothrombin time of 20 to 25 seconds is the range in which the prothrombin is decreased as much as is consistent with safety from hemorrhage.

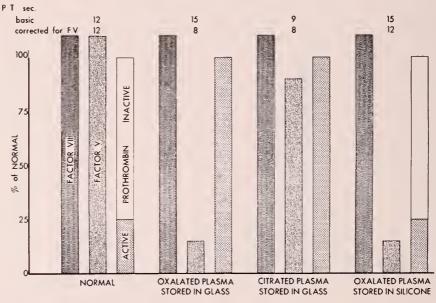
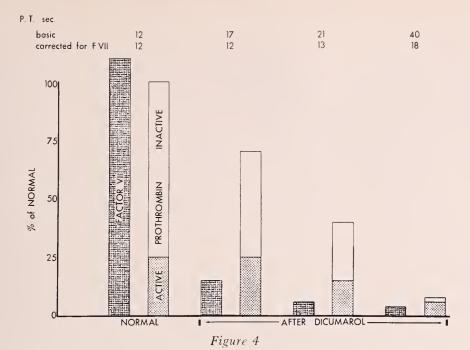


Figure 3

The effect of storage on factor V and the activation of prothrombinogen. When factor V drops below a critical level, it becomes the determinant of the prothrombin time. When factor V is restored, the prothrombin time is a measure of the free prothrombin. In citrated plasma, little factor V is lost but all of the prothrombin is converted to the active state. In a silicone-coated tube, prothrombinogen is not activated, hence the prothrombin time of the stored plasma returns to 12 seconds when factor V is restored.



The relation of factor VII to prothrombin. The level of free prothrombin diminishes only significantly after factor VII is greatly depressed.

Factor X, also known as the Stuart-Prower factor, is classified with the factors of the prothrombin complex because, when deficient, the prothrombin time is increased. It can also be placed in Step two because it appears to be essential for the generation of thromboplastin. Like factor VII, it is present in normal serum and becomes reduced after prolonged and intensive anticoagulant therapy. The one case of hereditary factor X deficiency studied in our laboratory is a mild bleeder whose prothrombin time is 16 seconds.13 It is normalized by aged serum. The prothrombin consumption is low and by means of the thromboplastin generation test the defect is found localized in the serum. The relative clinical importance of factor X deficiency is still to be established and awaits better methods for study.

#### Step 2

#### Generation of Thromboplastin

Characterizing test: Prothrombin consumption

Factors: Erythrocytin
Factor XIII (antihemophilic
globulin, thromboplastinogen)
Factor IX (plasma thromboplastin
component, Christmas factor)

The prothrombin consumption time is an in-

direct determination of the thromboplastin generated during coagulation. It is measured by the amount of prothrombin remaining in the serum under standardized clotting conditions. Platelets, factors VIII and IX are the known agents which are essential for the production of intrinsic thromboplastin and which, when deficient, cause a defective consumption of prothrombin. The original basic prothrombin consumption test<sup>14</sup> is non-specific but with simple modifications can be made a quantitative test for each of the three known factors needed for the generation of prothrombin. (Table III)

The participation of the platetlets in the generation of thromboplastin and the quantitative

Table III

Differentiation of Thrombocytopenia, Hemophilias A and B by the Prothrombin Consumption Test

	Normal sec.	Thrombocy- topenia*	Hemor	philia* B sec.
Basic prothrombin		1/6.6.4	occ.	170.0.1
consumption time:	16-35	8	8	10
hemolysate** with added	45-60	50	8	10
hemolysate and serum†	45-90	50	8	60

\* Results recorded were obtained from patients who were severe bleeders.

\*\* 0.1 ml. of hemolysate added to 1 ml. of native blood. † 0.1 ml. of hemolysate and 0.03 ml. of aged serum added to 1 ml. of native blood.

measurement of their activity are discussed under Step One. Evidence has been obtained indicating that the immediate reactant in the generation of thromboplastin is actually erythrocytin which is a product of platelets. Erythrocytin can therefore fully substitute for platelets in the reaction. Hemolysate, an extract of erythrocytes, which contains a high concentration of this factor is therefore a valuable reagent in the study of the generation of thromboplastin. When a defective consumption of prothrombin is corrected by adding hemolysate to blood before clotting, the cause of the defect is localized in Step One.

Factor VIII, the plasma constituent deficient in hemophilia is detected by a defective consumption of prothrombin as determined by the basic test. The procedure is made a specific measure of factor VIII by adding hemolysate and aged serum to the blood before clotting because in this modification an excess of the platelet derivative and factor IX are supplied. By means of the basic prothrombin consumption time and the modified test, all but the very mild cases of hemophilia A can be detected and the deficiency of factor VIII estimated.

Deficiency of factor IX is also detected by a defective prothrombin consumption time which is not corrected by the addition of hemolysate alone but which is by hemolysate and aged serum because the latter reagent supplies an excess of factor IX. The differentiation of hemophilia A from the B type is thus readily made. <sup>17</sup> (Table III)

#### Step 1

#### Activation of a Contact Factor to React

with Platelets

Characterizing test: Prothrombin consumption

time
Factors: Platelets
Contact factor

When platelet-poor plasma from a normal subject is clotted in glass, no measurable amount of prothrombin is consumed, but when a platelet extract is added prior to clotting, utilization of prothrombin becomes normal. If the platelet extract is added to plasma that has been in contact only with a silicone-coated surface, no consumption of prothrombin occurs. If the plasma is exposed for a short time to glass, or if a small

amount of thrombin is added, then the addition of platelet extract brings about a good consumption of prothrombin. This clearly suggests that a factor is present in plasma which, on activation either by contact with a glass surface or by thrombin, reacts with platelets, making them available for the generation of thromboplastin. It appears likely that the product thus formed is similar or identical to the clotting agent present in erythrocytes which has been named erythrocytin. The latter can participate directly in the generation of thromboplastin without the contact factor, whereas platelets must first react with the activated contact factor.15 Little is known about the latter and, so far, no clotting abnormality associated with the contact factor has been established. This factor should not be confused with the Hageman factor, which in some manner presumably participates in the activation of factor IX.

The important factor in Step One is the platelet. The bleeding tendency in thrombocytopenia is well recognized. Its diagnosis is made on the basis of the platelet count. When the platelets are functionally normal, the prothrombin consumption is found to become reduced below normal when the count is about 50,000/mm and then continues to drop proportionally, according to the further decrease of platelets.

A condition less generally recognized is one which may be classed as a type of thrombasthenia. The platelets are defective in quality when measured by the prothrombin consumption test. Patients with this abnormality have a bleeding condition similar to that observed in thrombocytopenia. The diagnosis of this bleeding state is often missed because the standardized prothrombin consumption test is performed in relatively few hospitals.

#### Discussion

The diagnosis of a hemorrhagic disorder, like that of any other disorder, is made on a careful correlation of history, physical examination and laboratory findings. The last of this diagnostic triad is of special importance in the bleeding dyscrasias.

Any average hospital laboratory can carry out correctly the few simple key tests with which the common bleeding states can be diagnosed. Standardized clotting and bleeding times should be done but their limitations recognized. If a firm clot is obtained, fibrinogen may be dismissed as a causative factor of bleeding. Normal clot retraction is a good indication that the platelets are numerically normal.

The two most important tests for localizing the clotting defect are the prothrombin time and the prothrombin consumption test. If the one-stage prothrombin time is normal, abnormalities in Step Three can be ruled out. When the basic onestage test is prolonged, the specific factor responsible can be identified and quantitatively estimated by simple modifications of the test.

The prothrombin consumption test, when found abnormal, places the coagulation defect in either Step One or Two. Again, simple additions to the basic prothrombin time make it possible to identify which factor is deficient. The basic test is not as sensitive as the one-stage prothrombin time; nevertheless, all but the very mild cases of hemophilias A and B can be detected with it and differentiated by simple modifications of the basic procedures. A modified prothrombin consumption time has been developed for the precise assay of factor VIII.16

The primary usefulness of nearly all the tests including the clotting time, the one-stage prothrombin time, the prothrombin consumption test and the thromboplastin generation test is diagnostic. Caution must be exercised in interpreting the findings of any test as a measure of hemostasis. This is clearly demonstrated by the clotting time. When found to be 30 minutes, it is indicative of a serious bleeding state when caused by a deficiency of factor VIII, i.e., in hemophilia, whereas when brought about by the Hageman trait, the clotting time has no hemostatic significance. Similarly, a prothrombin time of 30 seconds due to prothrombin deficiency brings about a serious bleeding tendency, while the same abnormal value caused by factors V or VII is entirely subclinical.

Exact diagnosis is of immediate importance because rational therapy is dependent upon it. Any laboratory which does the one-stage prothrombin time correctly, with a little additional effort, can do the prothrombin consumption test, and with this armamentarium is equipped to diagnose all but the more difficult cases, which fortunately are

The broad functions of the clotting mechanism and the physiological role of the various factors participating in or affecting the clotting reactions are still poorly understood. This problem will long remain a challenge requiring the coordinated efforts of investigators in many disciplines.

#### Summary

The clotting mechanism plays an important but poorly understood role in hemostasis. Useful information for correlating clotting with control of bleeding is obtained by the quantitative estimation of the various established factors that participate in the clotting reactions. For convenience and simplicity, the clotting mechanism may be divided into four major steps: 1, the initiating reaction (the generation of erythrocytin); 2, the generation of thromboplastin; 3, the generation of thrombin, and 4, the conversion of fibringen to fibrin. The key tests for characterizing these steps are: the prothrombin consumption time, the onestage prothrombin time, and the thrombin time. With these simple tests which should be routine hospital laboratory procedures, the diagnosis of most of the hemorrhagic diseases can readily be made.

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#### Present Indications for Surgery

#### in Congenital Heart Disease

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"The indications for surgical repair of congenital cardiac malformations . . . change from year to year . . . as the improvement in surgical techniques and in mechanical devices gradually decrease the operative risk, and as knowledge of the natural life history of the various anomalies grows."\* Because it has been three years since we last reviewed this topic, it is timely to do so again.

Perhaps the most significant changes in indications for surgery have been seen in the very small infant. Under most circumstances, open-heart procedures in this age-group still carry a high risk; however, certain palliative procedures have been evolved, which allow survival to a more optimal age and size. Though some other centers are doing complete repair of ventricular septal defects in the very small infant, we are performing pulmonary artery banding procedures in the small infant with congestive failure, very large left-to-right shunts, and normal or low pulmonary resistances. Sometimes it is possible to carry these infants along with scrupulous medical management; many will undergo spontaneous improvement at twelve to eighteen months of age, and will then remain free of life threatening trouble, although incapacitated, until a more reasonable age for open-heart repair.

In many, for one reason or another, it seems quite doubtful that survival to a year of age with medical management alone is to be expected. If catheterization reveals a large shunt and normal or low pulmonary resistance, the infant is a candidate for banding. In this procedure, a tie of umbilical tape is placed around the main pulmonary artery, compressing it to the point at which pulmonary artery pressure is normal and the shunt is all but obliterated; in most infants this can be done at the cost of a moderate elevation of right ventricular pressure and work.

#### Simple Operation

In effect, the infant is converted to a tetralogy with little shunt in either direction. It is a short, relatively simple operation. Gratifying relief of pulmonary congestion and left ventricular failure have been achieved by this procedure. When the child is much older, the band is then removed and open-heart closure of the septal defect carried out.

This procedure has been of value also in other more complicated malformations in which high flow-low resistance situations are present in the lungs; selected cases of truncus arteriosus, and tricuspid atresia with transposed vessels are examples. In these, the banding procedure was done to relieve severe symptoms and to prolong life, in the hope that, before deterioration of the patient occurs, a more definitive operation is available—a not unreasonable hope in these days of rapid advances in this field.

In the same category is the anastamosis of the superior vena cava to the right pulmonary artery. This is a closed-heart procedure, although occasionally a pump is employed to support the patient during the surgery. It is designed to increase pulmonary blood flow in cases in which a subnormal flow to the lungs is responsible for serious

<sup>\*&</sup>quot;Indications for Open Heart Surgery in Congenital Heart Disease."
published in Southwestern Medicine, Dec. 1958.

anoxic symptoms, such as in Ebstein's malformation of the tricuspid valve, in tricuspid atresia, and in pulmonary atresia with intact ventricular septum. Although only a palliative measure, it can make a child far more comfortable and prolong life, a prolongation which in some patients still remains indefinite.

In small infants again, a better understanding of the role of venous obstruction and of associated difficulties, such as a small left atrium, have made the surgical outlook in various types of total anomalous pulmonary venous drainage far more optimistic than in the past.

#### Surgical Feat

A surgical feat within recent years has been the accomplishment of total repair of complete transposition of the great vessels. Though the mortality rate of this procedure is still high, it has been demonstrated that total repair is indeed possible; it is to be expected that the technical problems responsible for the current high risk will be solved and the mortality reduced. The most spectacular element in this success has been the employment of profound hypothermia (5 to 10 degrees C.) and complete suspension of all circulation (even the extracorporeal mechanical one), permitting extensive surgical re-arrangement of the interior of the heart. Some are still being content with partial corrections, which, too, have been of noteworthy value and have significantly prolonged life expectancy in this common (eight per cent of all cardiac malformations) and challenging disease.

Thus, the age for possible salvage is being advanced nearer and nearer the newborn nursery. It therefore becomes increasingly important to establish a working diagnosis as to type of malformation at a younger and younger age. This is being accomplished by refinement in clinical diagnosis and increasing accuracy and decreasing risk in physiologic investigation in this fragile age-group.

Equally startling have been the advances in surgery in the older child. The repair of a secundum type of atrial septal defect is now accompanied by a mortality of less than one per cent; there are many centers, including our own, which have never lost a case. Our current criterion for surgical repair of this defect is the presence of

the disease, because of the usually relentless advance of pulmonary hypertension in the third and later decades of life; the optimal age for surgery is three to six years.

Our current indications for repair of a ventricular defect are tempered not only by the decreasing mortality in its surgery, but also by surprising disclosures of its life history. It is now considered as proven that:

- 1. An occasional small and a rare mediumsized defect will spontaneously disappear (catheter-proven before-and-after).
- 2. The development of progressive pulmonary hypertension in childhood, a dreaded complication, does occur but is unusual—probably occurring in less than five per cent of cases. The incidence of the complication in adult life is still uncertain.
- 3. Other changes can occur: progressive right ventricular hypertrophy can include outflow tract hypertrophy, changing the situation to a ventricular defect plus infundibular stenosis—i.e., a tetralogy of Fallot—a change which makes surgery more complicated.
- 4. Survival to a normal life expectancy still remains an unusual and unpredictable occurrence, although it certainly does occur.
- 5. Surgical mortality is greatly influenced by the development of complete heart block, due to trauma to the bundle of His; this complication can usually be avoided by the careful placement of sutures, and, as yet, has not occurred at our center.
- **6.** The overall surgical mortality should be less than five per cent.

Because of these shifting and opposing factors, we are still reluctant to recommend surgery in all ventricular defects, but urge it if there is:

- 1. Moderate or marked cardiomegaly,
- 2. A left-to-right shunt of two to one or more, or
- **3.** Evidence of infundibular hypertrophy with some stenosis.

In general, indications for closure of a patent ductus arteriosus, a surgical procedure of minor risk, have changed little: all ducts should be operated. The optimal age is above three and before six years, but the operation should be performed at any age if left ventricular strain or failure is evident. The only contraindication continues to be the presence of fixed pulmonary hypertension, which can be suspected from evidences of right ventricular hypertrophy on the electrocardiogram and proven by catheterization (which should be done in the presence of the above mentioned EKG abnormality). In infants more and more ducti have been reported with systolic murmurs only.

All coarctations should be repaired, best at eight to twelve years of age. However, in the presence of markedly retarded body growth or left heart strain, we are now more inclined to recommend operation in the symptomatic young infant than previously, as more and more reports of adequate growth of the anastomotic site have been reported. Re-stenosis and the necessity of re-operation still occur, but can be accepted as a reasonable risk in the very sick infant. Casefinding at the optimal age can be advanced only if the palpation of the femoral pulses becomes a routine for every physician who examines children.

#### Formidable Task

The surgical repair of tetralogy of Fallot is still a formidable task, but is becoming less and less so. In the optimal age (at least five years) the risk is now small (10 per cent higher in the severely cyanotic, lower in the acyanotic), and surgery at this age is recommended without trepidation. In the child younger than this, and in the very severely cyanotic patient, we continue to recommend a palliative procedure should severe anoxic symptoms be present; the procedure of choice is a Blalock pulmonary artery subclavian anastomsis, as this shunt can be taken down without too much difficulty when total repair is carried out at a later age.

The old criteria for surgery in pulmonic stenosis remain unaltered: 1) the presence of severe symptoms, and 2) right ventricular pressure in excess of 90 mm. Hg. The EKG remains a useful tool in selecting patients meeting the second criterion for cardiac catheterization. A third indication has been added: marked retardation of body growth, even if right ventricular pressure is below 90<sup>2</sup>.

A wide variety of types of aortic stenosis are now differentiated; some are far more curable surgically than others; exact preoperative distinction between the types is still a difficult problem, but one which is being solved. This is a deceptive disease, in which sudden death can occur with normal heart size and an unimpressive electrocardiogram. The correlation between ventricular pressure and EKG evidences of ventricular hypertrophy true in pulmonic stenosis is unfortunately not seen in aortic stenosis, However, several developments have decreased the magnitude of this problem:

- 1. Surgical repair is becoming more feasible with ever lessening risk.
- 2. Left heart catheterization by various means (retrograde arterial catheterization; direct left ventricular puncture; left atrial puncture from the right atrium) is becoming simpler and less risky.
- 3. Preliminary reports suggest that certain vectorcardiographic findings (especially the maximal vector in the horizontal loop) carry high correlations with left ventricular systolic hypertension and valvular gradient, and should develop into a valuable aid in proper selection of patients in whom left heart catheterization should be done.

#### Comment

In re-reading his comments on this subject three years ago, it is of interest to the author that several predictions made at that time have come to pass: criteria for surgical repair in certain defects have been liberalized; the desperately ill infant is now surgically more approachable, demanding increased diagnostic accuracy at a younger age; and new operations, as for transposition, have changed previously completely fatal lesions to ones which are now considerably more hopeful. It is equally predictable that another few years will produce changes of similar magnitude.

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## Psychotic and Psychoneurotic States Treatment with Chlordiazepoxide\*

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Within recent years a great number of pyschotropic drugs have been introduced and administered to patients suffering from various forms of mental illness.<sup>1,2</sup> The management of anxiety, agitation, and manic states in psychoneurotic and psychotic patients has been greatly altered and facilitated with the introduction of these new drugs. The rauwolfia alkaloids and phenothiazine derivatives, widely and successfully employed in therapy of the psychoses, are potent drugs suited for treating the acutely disturbed patient.<sup>1,3</sup>

The management of the psychoneurotic and the less severely disturbed patient has been fairly successful with meprobamate, prochlorperazine, perphenazine and others when anxiety is the presenting symptom. However, use of these drugs is accompanied by frequent and often severe side effects such as hypotension, agranulocytosis, tachycardia, Parkinsonism and sluggishness with the phenothiazines, 1,4,6 and withdrawal effects, hypersensitivity reactions and drowsiness which may occur with meprobamate. 1,4,5 In spite of the numerous tranquilizing drugs available, the search continues for one with a broader range of activity in controlling moderate to severe degrees of anxiety without producing undesirable side reactions.

Chlordiazepoxide, a new psychosedative with a broad range of pharmacological activity, belongs to a new class of compounds and exerts three primary actions: tranquilization, muscular relaxation and anticonvulsant effect. It has tranquilizing properties similar to chlorpromazine and reserpine but lacks their autonomic blocking effects, and produces no extrapyramidal side effects. It has a stronger muscle-relaxant effect than meprobamate, blocking spinal reflexes at lower dosages.

Broad clinical studies with this unique and intensively investigated drug show it to be effective in treating a wide range of psychoneurotic disorders including all degrees of anxiety and tension states, agitated depression, alcoholism, obsessive-compulsive reactions and schizoid behavior disorders. Serve Clinical studies have demonstrated that chlordiazepoxide is an exceptionally safe drug over a wide dosage range. There are no reported instances of liver damage, jaundice, blood dyscrasias, or physiologic habituation. Side effects, usually mild, are often reversible with dosage adjustment. Serve

The present study is concerned with a group of psychiatric patients and their response to treatment with chlordiazepoxide in various psychoneurotic and psychotic disorders.

#### Methods and Materials

Chlordiazepoxide was administered to 130 psychiatric patients (40 males and 90 females) ranging in age from 16 to 75 years, with a variety of psychotic and psychoneurotic disorders including anxiety and mixed psychoneuroses, reactive depression, schizophrenic reaction, schizo-affective

<sup>\*</sup>Librium, Hoffmann-La Roche, Inc., Nutley, N. J.

reaction, depression and others summarized in Table I. Routine physical examinations and laboratory tests were performed on all patients prior to treatment with chlordiazepoxide.

Seventy-eight patients had previously received other medications including glutethimide, hydroxyzine, trifluoperazine, meprobamate, isocarboxazid, disulfiram, chlorpromazine, mepazine, oxanamide, sodium pentobarbital, and others. Most of these patients had previously taken more than one tranquilizer and an overall response to treatment with these is summarized in Table II and compared with chlordiazepoxide.

mained symptom-free for the entire duration of treatment.

#### Results

Results of treatment with chlordiazepoxide are summarized in Table I. Twenty-eight patients or 22.2 per cent of the patients had an excellent response and 48 or 38.1 per cent had a good response. A fair response was noted in 14 (11.1 per cent) and 36 (28.6 per cent) showed no improvement while taking chlordiazepoxide. There was no follow-up in four patients. Remission of symptoms was obtained in 12 patients with anxiety

TABLE I
Summary of Results of Treatment with Chlordiazepoxide

	Nf	Response				No
Diagnosis	No. of Cases	Excel- lent	Good	Fair	Poor	follow up
Anxiety reaction	12	8	2		2	
Reactive depression	25	9	9	2	4	1
Depression	44	5	21	7	10	i
Conversion reaction	3		-		3	
Alcoholism	2		1	1		
Anxiety psychoneurosis	7	2	3	2		
Mixed psychoneurosis	9	2	3	1	3	
Schizoid personality	3		2			1
Schizophrenic reaction	5	1	1		3	
Schizoaffective reaction	6		3	1	2	
Paranoid schizophrenic						
reaction	4		1		2	1
Miscellaneous	10	1	2		7	
TOTAL	130	28	48	14	36	4
		22.20%	38.1%	11.1%	28.6%	

Dosage ranged from 10 mg. daily in two patients who obtained a satisfactory response at this dosage level to 75 mg. daily in several patients requiring a higher dosage. For most patients the dosage was 10 mg. given either two, three or four times daily. Duration of treatment ranged from one day to five months, with about three fourths of the patients taking the drug for a month or longer. Seventeen patients received adjunctive therapy with chlordiazepoxide. Iproniazid, methscopolamine, isocarboxazid, glutethimide, and chlorpromazine were the drugs given.

Evaluation of results was based upon subjective improvement and classified as excellent, good, fair, poor or no follow-up. Responses were not rated as good or excellent unless patients rereactions, eight of whom had excellent results, two good and two poor. Five out of seven patients with anxiety psychoneurosis also responded favorably to treatment with chlordiazepoxide.

Treatment of the various schizophrenic reactions was not as successful as in the anxiety reactions and depressions. Hysterical personality, gastrointestinal psychosomatic reaction, multiple sclerosis, and obsessive-compulsive reaction, all listed under miscellaneous, were among the symptoms that were only slightly relieved. Aggressive personality and migraine headache (under miscellaneous) were the two diagnoses in patients who had a good response to chlordiazepoxide; one patient with involutional depression showed an excellent response.

TABLE II

Comparison of Results of Treatment with Chlordiazepoxide and Other Medications

Diagnosis	No.	Previous medications				Chlordiazepoxide			
	Cases	Good	Partial	Poor	(Blank)	Good	Partial	Poor	(Blank)
Anxiety reaction	6	1	2	1	1	6			
Reactive depression	12	3	5	3	l	9	1	1	1
Depression	34	12	15	3	4	23	5	6	
Conversion reaction	2		1		1			2	
Alcoholism	1			1		1			
Anxiety psychoneurosis	4		4			2	2		
Mixed psychoneurosis	6		4		2	4		2	1
Schizoid personality	1				1	1			
Paranoid schizophrenic									Į.
reaction	3		1	1	1	1		2	γ.
Schizophrenic reaction	4		1	2	1	2		2	
Schizoaffective reaction				2	1	2		1	1
Miscellaneous	5		1	3	1	1		4.	
TOTAL	78	16	34	16	(14)	52	8	20	(1)

Onset of action varied from two days to two weeks, and was approximately seven days in most of the patients observed.

Table II summarizes patient response to chlordiazepoxide compared with the response to previously administered tranquilizers. It is evident that chlordiazepoxide was superior to the many different tranquilizers previously prescribed.

Side effects were infrequent and not serious. Ataxia, the most serious, was observed in six patients but in only two patients was it necessary to discontinue medication. Chlordiazepoxide was continued for five months in one of the other four patients, three months in two and one month in one, and results were excellent in one patient, good in two and fair in one, illustrating that even in the presence of slight ataxia, good results could still be obtained. Drowsiness which occurred in eight patients disappeared in five when the dosage was lowered, and was not incapacitating in the other three patients who continued taking the drug for longer than a month.

Two patients developed a skin rash, which was transient in one patient but serious enough in the other to require discontinuation of the drug. Decreased libido occurred in two patients. Hypotension, urinary incontinence, and dizziness were each observed once. One patient experienced extreme agitation after taking chlordiazepoxide for one day and refused to continue treatment. In this case, however, it is questionable whether the agi-

tation was due to the effects of chlordiazepoxide.

#### Discussion

The results obtained with chlordiazepoxide in this group of psychiatric patients compare well with similar studies with the drug in disorders in which anxiety was a prominent component. 8-11 In this series of patients, best results were obtained in the relatively uncomplicated anxiety reactions. It was also effective in other neurotic reactions and depressions and was of least and perhaps little value in schizophrenic reactions.

The use of chlordiazepoxide in the management of schizophrenia is not clear,<sup>13</sup> although it has been reported to be of value in treating some cases.<sup>14,15</sup> Compared with the effectiveness of many different tranquilizers previously administered to 78 patients in this study it is apparent that chlordiazepoxide is a unique as well as effective drug. Equally or more effective than many of the currently used tranquilizers, chlordiazepoxide has also a wide margin of safety.

Such side effects as occur are often reversible with proper dosage adjustment and are rarely serious when they persist. It is interesting to note in this study that even in the presence of ataxia, some patients continued the use of the drug with good results. Based on its effectiveness in this series of patients, many of whom failed to respond to previous medications, and the absence of serious side effects, it appears that chlordiazepoxide is a

worthy addition to the currently available tranquilizing drugs.

#### Summary

Chlordiazepoxide was administered to 130 psychiatric patients with a variety of psychotic and psychoneurotic disorders. Dosage ranged from 10 mg. daily to 75 mg. daily with most patients requiring 10 mg. given two, three, or four times daily. Duration of treatment ranged from one day to five months with about three-fourths of the patients taking the drug for a month or longer.

Twenty-eight of the patients had an excellent response, 48 a good response, 14 a fair response, 36 showed no improvement and there was no follow-up in four.

Patient response to chlordiazepoxide was superior to that of previously administered tranquilizers which 78 patients had received.

Side effects were infrequent and not serious. Four patients discontinued the drug due to the side effects. Two of these had ataxia and one patient developed a skin rash. Another patient experienced extreme agitation after taking chlor-diazepoxide for one day and refused to continue treatment. Other side effects either disappeared when the dosage was lowered or were not severe, e.g. dizziness.

It may be concluded from the study of chlordiazepoxide in this series of patients that the drug is an exceptionally useful drug in the treatment of a wide range of psychiatric disorders.

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SOUTHWESTERN MEETING HEADQUARTERS—Headquarters for the 44th annual meeting of the Southwestern Medical Association in Albuquerque, Oct. 18-20, 1962, will be the Western Skies Hotel, shown below.



#### Border Health Problems

The Mexico-U.S. Border is the most traveled one in the world, with an estimated 100 million crossings per year. El Paso-Ciudad Juarez, where about one fourth of these crossings occur, is the world's number one international port of entry.

The Border Field Office of the Pan American Sanitary Bureau was established at El Paso in 1942 as an international health agency at the service of both nations in improving public health in the border region.

Some of the border area's outstanding health problems are: control of communicable diseases such as tuberculosis, smallpox, and venereal diseases; control of those diseases (zoonoses) which are transmitted between animals and men, such as rabies, anthrax, "Q" fever, and brucellosis; and the betterment of environmental health through improved water supply, sewage disposal, and occupational health.

The Mexico-U.S. Border Public Health Association was founded in 1943. Like the Field Office, its object is to facilitate the improvement of public health along both sides of the border. The Association today has a membership of 900 public health officials from the six Mexican and four U.S. states that front onto the border. Its membership includes nurses, sanitary engineers, veterinarians, and other health officials as well as physicians. Through the Association members are able to exchange experiences, discuss mutual problems, and develop the personal and professional ties that are so important to the successful completion of all international health projects.

#### M. D. Sued, Sues Attorney

Doctors who have experienced unjustified suits for alleged malpractice might draw some satisfaction from the turnabout success of a California colleague.

Having successfully defended a malpractice suit, he rebutted with a suit against the claimant's attorney for giving a newspaper reporter "false information" about the case.

The doctor was awarded \$18,500 damages in Long Beach Superior Court.

-New Mexico Medical Society Newsletter

#### Coming Meetings

New Mexico Chapter, American Academy of General Practice, Summer Clinic, Ruidoso, N. M., July 16-19, 1962.

University of Colorado School of Medicine, Postgraduate Course, Dermatology for General Practitioners, Denver, July 19-21, 1962.

The Western Association of Railway Surgeons, annual meeting, Stockmen's Motor Hotel, Elko, Nev., Sept. 27-29, 1962.

Southwest Obstetrical and Gynecological Society, 12th Annual Meeting, Camelback Inn, Phoenix, Oct. 10-13, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.

Southwestern Dermatologic Society, Annual Meeting, Western Skies Hotel, Albuquerque, October 21, 22, 1962.

American Cancer Society, 1962 scientific session, Biltmore Hotel, New York, Oct. 22, 23, 1962.

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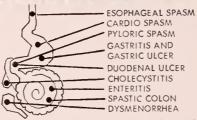
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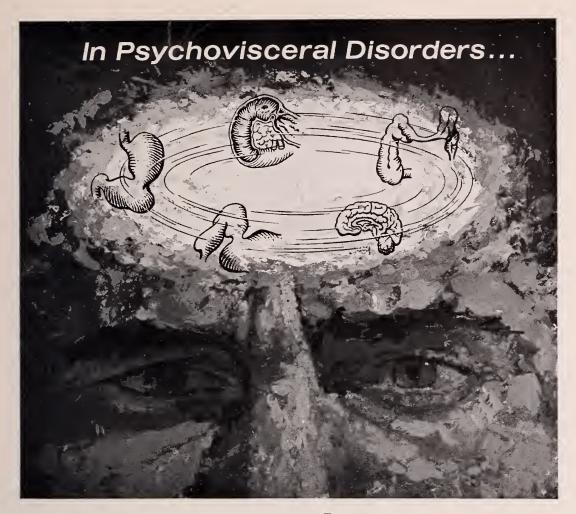




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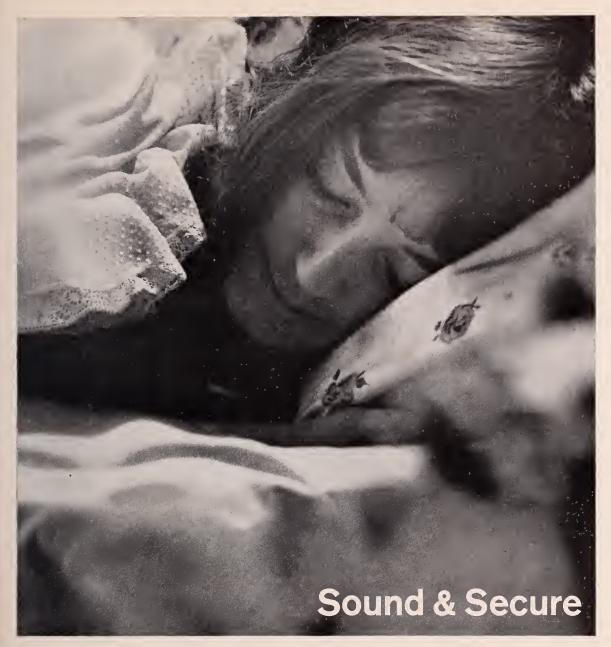
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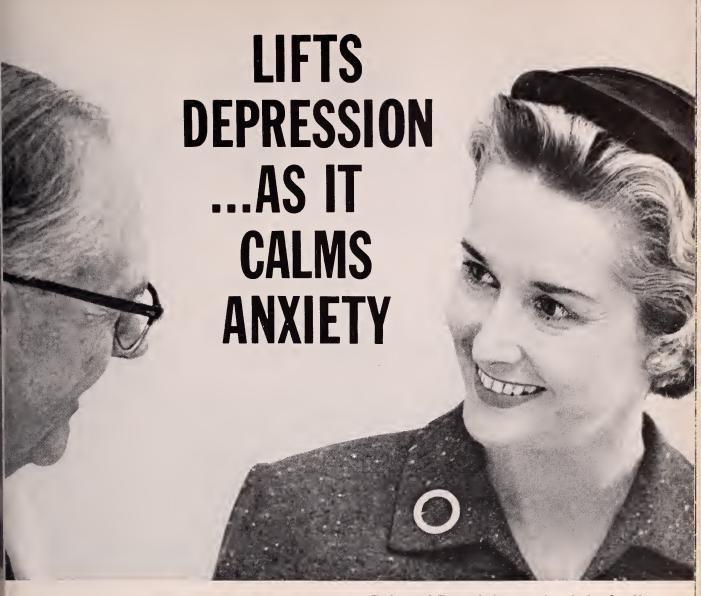
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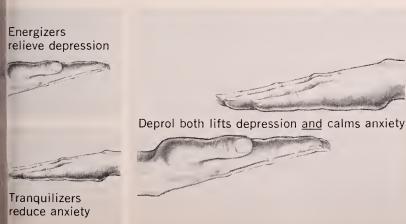


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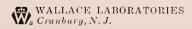
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Third annual Methodist Hospital Lectureship in Internal Medicine, Pioneer Hotel, Lubbock, Texas, Sept. 29, 1962.

Southwest Obstetrical and Gynecological Society, 12th Annual Meeting, Camelback Inn, Phoenix, Oct. 10-13, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.

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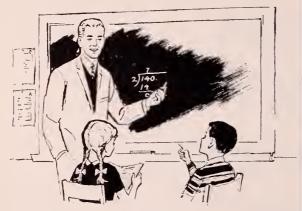
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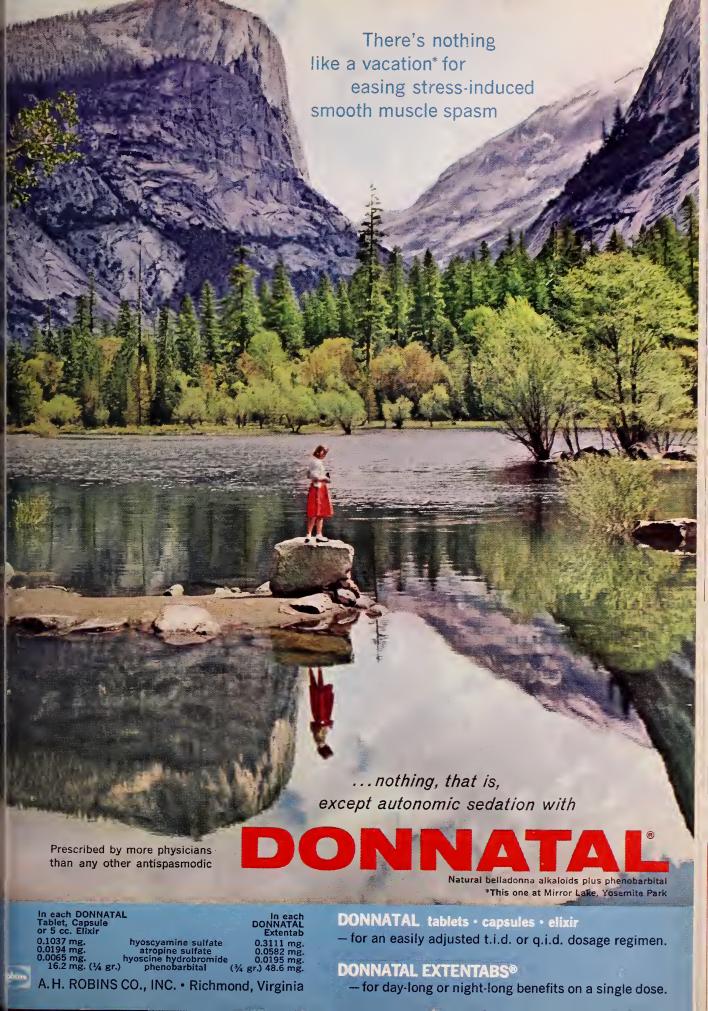
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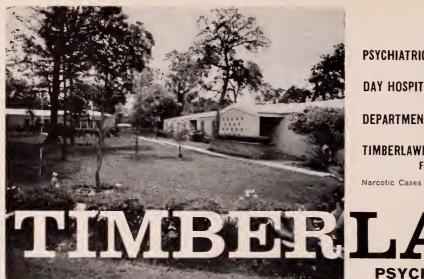
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# Santa Fe Seminar

## Surgical Lesions of the Colon

St. Vincent Hospital, Santa Fe April 24, 1962

Presentation by: Richard M. Angle, M. D.

Discussion by: Edward S. Judd, M. D., Mayo Clinic, Rochester, Minnesota

#### Dr. Angle:

Case #1 Record No. 42181 Mrs. A. B. Age 57

First Admission: 6/2/54 to 6/24/54. P. I. October, 1953 bleeding from rectum. Hemorrhoid found by her physician. Relieved with suppositories only to recur April, 1954. X-rays showed ragged filling defect of upper rectum. Sigmoidoscopy: Villous adenoma. Five biopsies showed no malignancy. Operation 6/4/54: Local resection for villous adenoma and colostomy. Uneventful recovery except for phlebothrombosis.

Second Admission: 7/25/54 to 8/3/54. Closure of colostomy; uneventful.

Third Admission: 12/29/57 to 1/8/58. Frequent sigmoidoscopes had revealed no evidence of recurrence until 12/17/58 recurrence at suture line, confirmed by biopsy. Lesion eight cm. above the anal margin. 12/30/57: Posterior proctotomy, excision of villous adenoma.

Fourth Admission: 9/14/58 to 9/16/58. Small recurrence found seven cm. above the anus. 9/15/58: Excision and cauterization. Again no malignancy.

Fifth Admission: 10/15/61 to 10/19/61; Extensive surface recurrence. Biopsy still showed no malignancy. Extensive cauterization. Patient last examined in March, 1962; no evidence of recurrence.

Dr. R. C. Derbyshire: The radiologist reported this filling defect which Dr. Wyloge will show you and asked if the patient had been proctoscoped. I indignantly said, "Yes, of course she was" and immediately afterward when she climbed back up on the table which she had been doing at frequent intervals I saw the lesion. I mean, this is just an example of the trap you can fall into with a large rectal ampulla in not manipulating your instrument carefully enough and I apologize for the radiologist, who I think was Dr. Wyloge, making this diagnosis.

**Dr. Judd:** Dr. Derbyshire very kindly showed me these films this afternoon and I would like to commend the roentgenologist on having caught this at an area which frequently is a relatively blind spot in our experience.

Dr. Elliott I. Wyloge: This was the initial filling film of the rectal pouch and I think it well demonstrates the large irregular filling defect on the right lateral wall of the rectal pouch. Additional films of that area show the lesion as quite ragged and polypoid in nature and rather long in extent, and in this film which is the Chassard-Lapine position, you see the extent of the lesion and the irregularity of the lesion on the right side of the rectal pouch.

Sante Fe Seminars are supported by a grant from the Merck Sharp & Dohme Postgraduate Program.

Dr. Judd: I want to comment that I would certainly not quarrel with the treatment that was selected here at all. We see this type of case frequently. It, to all intents and purposes, is a benign lesion. Now, it does have a nasty habit of recurring even after repeated fulgurations. These people still come back and they'll have soft, yielding, peculiar feeling polyps in the rectum. Unfortunately they are so often in the distal segment.

Notice here that this one recurrence was seven cm. from the anus. Well, that commonly would require radical sacrifice of the entire rectum and all sphincters. We do not do routine combined abdominoperineal resections for villous adenomas. I am fully aware that in certain centers they demand that this be done. The difficult situation in my experience has been, that if we get a little piece through the proctoscope, which is analyzed in our laboratory and found to be true villous adenoma, we might not have gotten down into the center of the lesion. We have removed a fair number of these which are villous adenomas around the periphery, but when we get the entire segment in the laboratory there can be invasive cancer in the center. That isn't the situation here, as I understand this case.

It has been about eight years now that this patient has been carried along with normal fecal control, and no sign of cancer as of 1962. I think that I would agree 100 per cent with the treatment that has been selected here, although I am fully aware that others might feel that the sacrifice should have been carried out. I think she might have been mutilated.

Dr. Angle: Dr. Derbyshire, do you have any comments?

Dr. Derbyshire: No, except that I would like to ask Dr. Judd one question. Do you think that these lesions are somewhat similar to warts, possibly? I am not talking about hypnosis in treatment of villous adenoma, but this last operation was extremely unsatisfactory. This woman had an extensive recurrence at the last fulguration, and I told her that I had not gotten all of it. I cauterized for about an hour-and-a-half and finally got choked with the smoke, I think, and quit. I told the patient that I hadn't gotten it all and that she was going to have to come back, which she was

perfectly willing to do. She returned to the office for sigmoidoscopy three weeks later and I couldn't even tell where the lesion had been. It was completely cured and I know I didn't get it all. Is there any explanation?

Dr. Judd: I don't have the explanation. I think it is very similar to the plantar wart and I know that's a very difficult thing to cure, although it's considered a benign condition. We have had the same experience as you, and when patients come back for a check-up we expect quite a nasty situation but it looks pretty good.

Dr. Angle: Dr. Judd, Dr. Wyloge has the films of the recurrence.

Dr. Wyloge: The films on the right were made in December, 1957, and the lesion is again visualized on the right side of the rectal pouch. It's about half the size it was previously but it still shows the same polypoid characteristic. In addition the rectal pouch is somewhat narrower than it was before and I assume that these changes are all postoperative in nature.

Dr. Harry D. Ellis: How did it happen that an abdominoperineal resection wasn't done?

Dr. Derbyshire: I agreed with Dr. Judd. There had been five biopsies and not one of them showed carcinoma. I didn't feel justified in doing the mutilating procedure.

Dr. Angle:

Case #2 Record No. 42045 Mr. E. R. Age 70

Admitted 8/23/61 to 10/10/61. P. I. Abdominal cramps with increasing distention for 1 week. Ribbon-like stools for 2 mo. prior to this. Physical examination: Huge abdominal distention, tenderness. X-ray: Closed loop obstruction of large bowel. 8/23/61; Emergency transverse colostoniy, complicated by coronary thrombosis. Later barium enema showed diverticulitis. Last seen in March, 1962, condition good, has gained 20 lb. Still has colostomy.

Dr. Wyloge, may we see the films, please?

**Dr.** Wyloge: These films made on 9/27/61 showed a marked narrowing of the mid-sigmoid area with a high degree of obstruction to the flow of barium as you can see. (Fig. 1)

Despite the fact that the patient had a balloon in the rectal pouch only a small amount of barium got beyond the long lesion in the sigmoid colon. At this time he experienced quite a lot of pain from the distention and he was unable to hold the



Figure 1

Case Number Two. Marked narrowing of midsigmoid area.

barium and in addition to being a rather difficult place to visualize, he was rather difficult to examine. But in spite of that, we let him rest for a few moments and then tried to instill some more barium in an attempt to evaluate the lesion and we see a constant irregular narrowing of the midsigmoid in the presence of multiple diverticula.

In addition we see what appear to be two tracts traversing the same area of the sigmoid, which I suspect represent a sinus tract or an inter-communication between several of the diverticula in that region. The area does change somewhat with spasm and contraction of the area and also at the time of the evacuation, and in this view where he is again sitting on the table you can see how long this lesion is, almost seven cm. in length.

A further attempt at depicting the lesion was done by introducing barium through the colostomy, after surgery, in an attempt to evaluate the area but there was also a marked degree of obstruction to the downward flow of barium through the colostomy. It was the conclusion at this time that this was a zone of a diverticulosis with diverticulitis and presumably perforation and sinus tract formation in the mid-sigmoid. One is always skeptical at this time whether one has ruled out the presence of malignancy in diverticulitis because a tumor frequently has the same appearance.

Dr. Angle: Thank you, Dr. Wyloge. Dr. Judd.

Dr. Judd: I would certainly agree with what Dr. Wyloge has said on the length of the segment. You can see what a long region is involved with a relatively minor amount of nucosal change, if any, and we are all worried about cancer being present. Yet all these indications seem to point to benign diverticulitis. I would certainly not be concerned about the continuing colostomy if the patient does reasonably well with it. Many people who have a benign lesion of the colon, and know it, and have an intact rectum, will really be concerned until they once again have a normal continuity re-established.

My suggestion for this man, since the operation was done in October, would be to check him again by x-ray after three to six months to see if there is continuing subsidence of these changes, because I think then we can assume that it is definitely diverticulitis. He is over 70 years of age, he probably has other intercurrent diseases and he is not too upset about the colostomy. I think I would just as soon leave it as is. Now, if he is a good risk and he is disturbed about the colostomy, I would certainly not hesitate to go ahead and resect. We usually wait at least six months in a case like this, where there is complete obstruction and a great deal of inflammatory change, because there can be abscesses present in the mesosigmoid even after three or four months.

It isn't necessary to wait six months, of course, in all cases, but it's better because the operation is easier and the resection can be accomplished with much less risk. It would be a temptation after six more months if this subsides (and it might subside just like magic and all you can see then is diverticulosis)—to close the colostomy, but our experience has been that in two-thirds of these individuals recurrent diverticulitis will develop and then we will be back in the same trouble again.

**Dr. Angle:** Thank you, Dr. Judd. Dr. Derbyshire.

Dr. Derbyshire: I only have one comment. Dr. Streeper and Dr. Johnson have made the patient very happy with his colostomy and they won't let me go ahead with any more surgery. I am sorry that we don't have the original films that Dr. Johnson sent from Las Vegas. I think they were returned to him. It was a spectacular case of closed

loop obstruction, very frightening to look at, and fortunately we were able to decompress it.

#### Dr. Angle:

Case #3 Record No 36560 Mrs. Z. S. Age 69

Admitted 8/12/60 to 9/3/60. First seen by internist 6/23/60 complaining of "gas" and nervous tension. July, 1960 onset of persistent watery diarrhea. Physical examination essentially negative. X-ray: Annular constricting carcinoma of transverse colon.

Operation 8/18/60: Chronic ileocolitis involving eight cm. of transverse colon, 12 cm. of terminal ileum. Incidental finding — polyp of colon. Resection and ileocolostomy end-to-end. Recovery uneventful except for agitated depression lasting two days. Last examined in office April, 1962. well, had gained 20 lb.

Dr. Friedman, may we see the x-rays?

Dr. Murray M. Friedman: This film shows quite clearly a rather long narrow segment with rather smooth margins in the mid transverse colon, reproduced in all of these films (Fig. 2). The mucosal pattern appears to be obliterated. Some barium passed into the terminal ileum and that doesn't look too bad.



Figure 2

Case Number Three, Long narrowed segment in transverse colon.

Dr. Angle: Thank you, Dr. Friedman. Dr. Derbyshire, would you like to comment on the findings at surgery?

Dr. Derbyshire: This patient had a segmental ileocolitis. She had about 12 cm. of terminal ileum involved with a skip area to the transverse colon which was also typical segmental colitis. I want to ask Dr. Friedman if, in hindsight, he would call that a "string sign" in the terminal ileum?

Dr. Friedman: There is a little point in one film that would qualify for that, perhaps, but looking at this other film here it is not present and so is an inconstant finding.

Dr. Angle: Dr. Judd, would you like to discuss this case now?

Dr. Judd: I take it that you resected the terminal ileum and the entire right colon around into the transverse. Was there no disease of the right colon?

**Dr. Derbyshire:** There was no disease of the right colon. Just the transverse colon and the terminal ileum with no skip areas above the terminal ileum.

Dr. Judd: That's rather unusual, of course. You'd expect that if the transverse colon were going to be involved like that, the right colon would be also; but not necessarily. We have seen them with ileitis changes way around in the sigmoid and the remainder of the colon entirely normal. Some of the pathologists feel that they can determine whether it's chronic ulcerative colitis or a secondary type of ileitis involving the sigmoid.

The great trouble here, of course, is what does the future hold? I am afraid that this patient may be headed for more trouble, because one very definite skip area has been demonstrated in the distal bowel. You would be looking for it going proximally in the small bowel. Possibly there is less chance of disease in the distal colon than there might have been had the skip area already been demonstrated in the proximal remnant of small bowel. This is quite an unusual case. She's doing well?

Dr. Derbyshire: Yes.

Dr. Angle: Dr. Ellis, would you like to say anything about the pathological picture you found in this woman?

Dr. Ellis: No.

**Dr. Derbyshire:** I would like to ask Dr. Judd one question. In case we have a recurrence in this case, what do you think we'd have to offer her, not surgically?

Dr. Judd: I don't think you have a great deal, really. The ones we see usually come in having had all kinds of steroids, with moon faces, buffalo humps and purple striae, and then we're really in

a bad way. You can't operate on them because they perforate the bowel and the bowel bleeds badly. Steroids can be greatly overdone. Now all of us have seen people tremendously improved by steroids which can be lifesaving. If we see recurrent disease in an area which might lend itself to re-resection we go ahead and resect.

Some of them have had four and five operations but we tell them before the first operation, very frankly, that recurrence is often a rule, that it may be a simple one-stage or a multiple-stage operation. Then we get into situations where the lesion won't heal any more. And even though the distal sigmoid and rectum are entirely normal, you can't seem to make the anastomosis hold. We have a few people who have ileostomies for ileitis which is not a very happy existence but it's better than continuing fistulae.

Dr. Derbyshire: Do you think that her age is in her favor? 71 now.

Dr. Judd: Yes, I certainly do. It seems to be a burned out lesion when you get them at that age. President Eisenhower's disease is certainly a fascinating thing. To have come on in the middle of the night with no preceding trouble as far as anyone knows and, as far as anyone knows now, he hasn't had any further trouble. I think we all would agree that in this patient, her chances, from age alone, are much better of remaining quite well.

**Dr. Angle:** Dr. Judd, I would like to ask you in regard to this case: Do you think that surgery was properly done or do you think that in hindsight we should have tried treating her medically with the degree of obstruction present?

Dr. Judd: I think you had to operate. I would agree 100 per cent here. The lesion was discovered perhaps at an early stage and the terminal ileum is out now and we know what it is and cancer has been ruled out. She is doing well. I think that it's very fortunate that you went ahead.

**Dr. Philip Shultz:** Dr. Judd, what would you think of an individual who has had a bypass ileocolostomy approximately five years ago with no active trouble? Do you think this individual should have a right colectomy or leave well enough alone?

Dr. Judd: We used to insist that they come back. The point is made here that the ileum was

isolated at the first operation, right? There was complete diversion. That must be done. Side-to-side ileocolostomy doesn't do much good in diverting the stream but many lesions will heal very nicely so that the large mass will disappear, they lose all their symptoms and to all intents and purposes are quite well. We used to insist that they come back to get all the disease out, but not anymore. If they are doing well, we leave them alone. Frequently we can still feel a little mass but we still leave them alone.

#### Dr. Angle:

Case #4 Record No. 44093 Mrs. J. C. Age 71

Admitted 9/15/57 to 11/10/57. Past history: Thyroid lobectomy in 1951 for benign adenoma. Gastric resection in 1955 for bleeding pyloric ulcer. P. I. For two months attacks of cramp-like abdominal pain lasting two or three days. Two days before admission severe pain, obstipation. One day before admission onset of vomiting. Physical examination: Slight distention, tympanites. X-ray: Marked gaseous distention of small bowel with fluid levels.

Operation 9/15/57: Side-to-side ileocolostomy for obstructing carcinoma of ascending colon. Severe post-operative wound infection. 10/28/57: Right colon resection. Uneventful recovery. Later developed large ventral hernia which was repaired on 3/7/62. Single nodule found in parietal peritoneum. Biopsy: Adenocarcinoma.

Shall we see the films first, Dr. Wyloge?

Dr. Wyloge: Examination of the abdomen in upright projections shows a large loop of small intestine lying in the mid and upper abdomen and several loops of small intestine. In the right abdomen in the upright position you see that these have varying-sized fluid levels, indicative of a mechanical obstruction of the small intestine. We have no subsequent films on this patient before her colectomy. All I have is a post-hemicolectomy study which shows the colon up to this point and from there on the small intestine with an ileo-transverse colostomy.

**Dr. Angle:** Dr. Derbyshire, do you have any comments at this point?

Dr. Derbyshire: Well, this case was presented mainly as a fairly unusual case of obstructing carcinoma of the right colon which we don't see too often. Also from the standpoint of management an emergency ileocolostomy was done which obviously was an unsatisfactory operation because the patient developed a severe wound infection which delayed the second stage for some four or five weeks. The outcome appeared to be good for

four years and I took a second look not long ago, the excuse being not advocating a second look procedure, Dr. Judd, but exploration was justified by the presence of a huge postoperative hernia which was causing a lot of trouble.

After the second look I was sorry that I had done so because she had a single nodule of recurrent carcinoma in the parietal peritoneum. I was not able to palpate the liver satisfactorily because of dense adhesions. I would like to ask Dr. Judd one question about the initial management of this case. Would you have considered an obstructive resection? Of course the proper diagnosis was not made preoperatively. We thought this was a small-bowel obstruction and I think even if you looked at this in hindsight, you could not say that it is an obstruction of the ascending colon. Would you comment on obstructive resection? Do you think it might be justified in a case of this type?

**Dr. Judd:** Did you have a long tube down to decompress the bowel?

Dr. Derbyshire: No, we did not.

Dr. Judd: I think that this is exactly what I would have done. A long tube might have been passed and have been successful. Of course the secret is to get the thing down and to have it work right. We can often get it down and get about 300 cc. of fluid out and then it quits working. The long tube is still something that is not 100 per cent perfect. You may be interested that at our University Dr. Wangensteen has now developed a coil-spring tube which can be passed and obviously will maintain a lumen no matter how many coils it takes and will continue to maintain suction through it so that it will decompress. It's a rather awesome looking gadget when you see it being passed but it will work.

In this case I would have done a side-to-side ileocolostomy. Dr. Derbyshire heaped some coals on his head about the wound infection, Well, you have to do something. You might have done a tube-type of decompressing Witzel enterostomy. There you are opening the bowel anyway and you are taking a certain amount of risk. To answer Dr. Derbyshire's question about an obstructive resection, which is merely a modified Mikulicz operation, which, as you recall, calls for delivering the tumor outside the abdominal wall — Mikulicz

simply left it there and put a hole in the proximal aspect of the bowel to decompress it and amputated the tumor, perhaps 10 days later.

The obstructive resection went one step further and amputated the tumor immediately at the first operation, leaving the patient with a double barrel colostomy because it was designed for the left side of the colon. The situation is very different in a 70 year old individual who is tremendously obstructed and perhaps depleted. Having the ileum become the proximal barrel of the stoma, there is constant discharge of the highly irritating small bowel content upon the skin of the abdominal wall and that is not tolerated at all well in either extremes of age, in babies or in elderly people. Wound healing then would have been very slow and electrolyte problems would have been great.

Now, I would have gone ahead and tried to get the bowel decompressed with at least one attempt on the long tube but I would have been ready to go right ahead and do a side-to-side ileocolostomy. As soon thereafter as the patient could be put into condition, I would do the definitive resection. Did you remove the metastatic nodule at the second operation?

Dr. Derbyshire: Yes.

Dr. Judd: People who have a completely obstructing carcinoma of the right colon have a rather poor outlook as far as the long term results are concerned. However, here is an individual who has had a second look where the malignant disease was removed and she may be one of the exceptions to the rule who dies of something else.

#### Dr. Angle:

Case #5 Record No. 20830 Mr. W. B. Age 76 Admitted 4/25/57 with painful growth and painful hemorrhoidal tags at the anus of one week duration. He had had an anal fistula operated in 1923. Biopsy done in the office revealed a squamous carcinoma of the anus. Physical examination revealed an elderly, rather frail man with severe glaucoma, fibrillation, moderate prostatic hypertrophy, edema of both ankles. There was an ulcerated tumefaction about 2 x 1 & ½ cm. on the right mucocutaneous border of the anus.

Laboratory findings non-contributory. Chest x-ray revealed sclerotic changes of the aortic arch. 4/26/57: Under spinal anesthesia, a block resection was carried out including the right half of the sphincter. The mucous membrane was undermined and brought down for closure. Pathology report revealed the tumor to be a grade II-III squamous carcinoma. This man had an uneventful postoperative course and is alive and well at this time.

Dr. Friedman, do you have any x-rays on this case?

Dr. Friedman: I have a barium enema examination which as far as we were concerned was normal except for the presence of a number of diverticula on the lower sigmoid colon.

**Dr. Angle:** Dr. Shultz, do you have any further comments on this case?

Dr. Shultz: I have nothing to add to the history only that at the time of surgery in 1957 we felt somewhat pessimistic as though perhaps we were doing an inadequate procedure in not doing a more radical Miles-type approach to this tumor. The tumor was localized and fortunately there has been no recurrence. He has had careful periodic followups.

Dr. Angle: Dr. Judd.

Dr. Judd: This is a wonderful result in my estimation — a five year cure of squamous cell disease of the anus. This can be a really malignant lifetaking disease in our experience. We have more recently gone ahead with early radical surgery which means a very radical combined abdominoperineal resection, accompanied immediately, or perhaps a little later, by bilateral lymph node dissection, which is a lot of surgery.

We have numerous people, though, that have never come to this and many of them have done well. I don't know how many five year results we have. They are treated frequently before we ever see them. They are treated by radium and x-ray and local excision and the surgeon always complains that he gets them after somebody else has messed them all up. That's not necessarily true at all. Everyone is trying to give the patient a decent break and to save the anus and to make it as safe a procedure as possible. Obviously in this case the exactly correct operation was selected for this man. He has a wonderful result.

Unfortunately, some of the early ones were seen after pruritus ani.

Before the days of carefully-controlled x-ray therapy, a great deal of x-ray was used for pruritus ani and this resulted in control of itching, but squamous cell carcinoma was engrafted upon the radiation changes around the anus. I'm not too sure how much good we do with the bilateral groin dissection. We reviewed a series of about 120 of these collected at our institution over a long per-

iod and found that when nodes were not involved, we had numerous excellent sounding results. However, when any nodes were involved, regardless of how radical we were in our surgical approach, we had no five year survival.

**Dr. Angle:** Dr. Shultz, do you have any further comments?

Dr. Shultz: I don't believe that this gentleman would have survived an abdominoperineal resection and was quite surprised that he had survived five years on his own. Dr. McGoey might have a comment.

**Dr. Charles J. McGoey:** By accident he was seen this afternoon. He remained something of a problem with the management of his congestive heart failure.

Dr. Judd: How is his fecal control?

Dr. Shultz: Excellent.

Dr. Angle:

Case #6 Record No. 44185 Mr. M. M. Age 50

Admitted 12/8/58 with a 10 year history of intermittent diverticulitis with pain, obstipation and lower abdominal tenderness. A repeat barium enema had revealed an increasing extent of diverticulitis with marked luminal narrowing in the sigmoid area. Physical examination and laboratory findings were essentially normal.

He was given a Neomycin — Sulfathaladine intestinal preparation and on 12/15/58 a sigmoid resection was carried out with an open anterior end-to-end anastomosis. The patient's postoperative course was wholly uneventful Pathology revealed: Chronic diverticulitis with two adenomatous polyps present in the specimen. The patient is alive and well at this time.

Dr. Shultz, have you any comments or shall we have Dr. Wyloge show the films?

**Dr. Shultz:** This patient shows nothing particularly unusual or abnormal and was included only because we wanted a case of diverticulitis.

Dr. Wyloge: The original studies on this patient began in 1949 at which time he had a barium enema well-demonstrating a large area of diverticulitis in the mid-sigmoid with a few diverticula in the proximal sigmoid, diverticula present in the descending colon and possibly a few diverticula in the hepatic flexure. As you see, in 1949, the area of the sigmoid shows non-contractibility in spite of the fact that there is marked spasm of the after-expulsion films.

In 1950 the patient had a barium meal and in a six-hour examination of the abdomen, barium is

distributed throughout the colon and the numerous diverticula are again seen in the colon, particularly in the descending colon and in the sigmoid region in which area he again shows spasm, but the tooth-like and saw-tooth appearance of diverticulitis is not present. He had a subsequent GI series in 1951, and again the six-hour film shows similar changes in the colon as noted previously. The last barium enema was made in December, 1958, practically 10 years from the original barium study, and again demonstrated the characteristic signs of diverticulitis of the sigmoid colon. The area again shows some degree of extensibility and non-contractibility with retention of stool in the region of the diverticulitis,

As noted on the protocol several adenomatous polyps were seen in the region of the diverticulitis and even in retrospect I don't think that we could make that diagnosis from the film study because of the presence of all the diverticula and of stool in the area. Here is a post evacuation study and aircontrast examination and because of the superimposition of all of the shadows I think it would be very difficult to make a diagnosis of polyp.

Dr. Angle: Thank you, Dr. Wyloge. Dr. Judd.

Dr. Judd: I certainly agree wholeheartedly with resection of the sigmoid colon for recurrent diverticulitis. I think that the day has passed when we are going to be neglecting these people. I can remember at our institution when these people were put in the hospital, given hot packs and a residue-free diet, a nasal tube and whatever the newest form of antibiotic or sulfonamide was, tided over the trouble and sent on their way, and then repeatedly they would go through this business.

Finally there would be an abscess, someone would drain this and following the evacuation of pus the surgeon would be horrified to see feces coming out of the abdominal wall. The abscess might burst into the urinary bladder, especially in men, and don't forget that in women who have had a hysterectomy the same problem exists and then it's a series of operations to get them straightened out.

When we see these people now—(and our internists are among our most enthusiastic supporters because they don't like to go through this thing either)—we do a primary one-stage resection. We thought we were getting somewhere but the other

day one of the orthopedists showed me a film. The patient had an abscess around the hip joint and he drained it, and the next day the bowels were moving through this incision around the hip joint. An x-ray of the colon showed a perforated diverticulitis. The orthopedist thought he was dealing with a gas-forming organism in his first x-ray, because there was gas surrounding the hip joint, but this was gas coming from the colon.

So we still see these cases but an orderly effective one-stage resection done ideally in the well-prepared colon is a small price to pay when the patient compares this with what he might be doing if he procrastinates. I think we are really making a great deal of progress. I would like to ask our moderator, Dr. Angle, about bleeding in diverticular disease. Do you think that diverticulosis or diverticulitis ever produces exsanguinating hemorrhage?

**Dr. Angle:** I have seen reports of this but I have never seen the actual condition. I was about to ask you how often you saw major bleeding in diverticulitis.

Dr. Judd: What we might find is that it is due to polyps. If this patient had bled profusely he might be signed out as hemorrhagic diverticulitis but Dr. Ellis found these polyps and immediately took him out of that category because no one can say that bleeding in this case would have come just from a diverticulum. We see the type of reasoning where a patient comes in, frequently an elderly patient, almost exsanguinated and bleeding finally stops. He is reconstituted on his blood and electrolytes and then we can do some studies.

We are then confronted with diverticulosis in the x-ray—not diverticulitis necessarily—but just diverticulosis. The medical men say, "Okay, fix this up". Well, what do you do? You go in and take out the sigmoid and where is the bleeding coming from? One of my senior colleagues, whose name would be very familiar to Dr. Derbyshire were I to mention it, went in and did this very thing, taking out the whole colon and saving the rectum. There were diverticula all the way around to the cecum and as he didn't have any idea where the bleeding was coming from he took the whole colon out and anastomosed the ileum to the rectosigmoid. Just before closing he could really look around and found a huge Meckel's diverticulum. We don't know the outcome!

Dr. Angle:

Case #7 Record No. 32669 Mr. P. Q. Age 59

Admitted 11/5/59 with a history of 40 lb. weight loss in the preceding four months with intermittent upper abdominal pain. No abnormal bowel habits or tarry stools but extreme fatigability. Physical examination revealed a markedly pale individual with a strange bronzing of his skin. There was a grade II-III blowing systolic murmur transmitted to the axilla. Abdominal examination was entirely negative.

X-ray work-up revealed cardiomegaly, primarily left ventricular. There was no calculus in the gall bladder and a filling defect was demonstrated in the cecum. Upper GI was negative. Electrocardiogram changes were interpreted as being due to right ventricular hypertrophy. This patient had an admission hemoglobin of 5.2 grams with 20 per cent CV and an RBC of 3,000,000, marked anisocytosis, poikilocytosis and hypochromia. Fecal occult blood positive.

This man received four preoperative transfusions and one at surgery. He was given Sulfathaladine colon prep and operated 11/19/59. The cecum was found to be high and fixed with a tunor present. A wide resection of right colon and transverse colon was carried out with an end-to-end anastomosis. The patient's postoperative course was totally uneventful. He was discharged 11/26/59 with hemoglobin of 15 grams. Pathology revealed adenocarcinoma. All of the lymph nodes in the specimen were negative for carcinoma. Patient is alive and well at this time.

Dr. Friedman, would you show the x-rays?

**Dr. Friedman:** The barium enema examination shows marked deformity of the cecum which proved in large part to be caused by spasm because after another effort we did manage to distend the cecum and demonstrate this filling defect on the lateral aspect.

Dr. Angle: It should be noted in the protocol that the patient had a marked iron-deficiency anemia, always a warning sign in a male or in a woman past the menopause. After four transfusions and another at surgery, the lesion was resected. Dr. Shultz, would you like to describe the surgical findings?

**Dr. Shultz:** For a change, this patient had a correct preoperative diagnosis of carcinoma of the cecum and this was proven at operation. The tumor was quite large and it was fixed to the posterior wall and a wide resection was carried out. I recall, the nodes in the resected mesentery were all negative for carcinoma. Again, this patient was seen just a few days ago and is alive and well.

Dr. Angle: Dr. Judd.

**Dr. Judd:** I was struck, in reading this over initially, by the "bronzing of the skin." It wasn't hemochromatosis, apparently?

**Dr. Shultz:** It was not. It wasn't pigment, but this has cleared.

**Dr. Judd:** Probably it was extreme pallor associated with anemia. This, of course, is the proper way to go about it, coming upon a case of severe anemia. Where do we start looking? The right colon is one of the very first places, assuming the patient doesn't have a peptic ulcer. For a while, many years ago, it was thought that perhaps there was some intrinsic factor that was disturbed, somewhat like pernicious anemia, because many of the blood smears revealed a peculiar hemogram that suggested a primary type of anemia.

Many years ago Dr. Will Mayo at our clinic put some of the young men to work grinding up the cecum and especially the mucosal surfaces of the terminal ileum wondering whether malignant tumors in this general area deranged some mechanism much as the atrophic gastritis that goes along with pernicious anemia due to the loss of the intrinsic factor there. Nothing was ever proved and apparently as it was borne out in this case, there is a continuing loss of blood which the patient himself doesn't appreciate. Blood loss goes on for a long period of time without changing the color of the stool and when the patient finally comes in he is tremendously depleted and many transfusions are required. This represents a very nice diagnosis and a very nice result.

Dr. Derbyshire: Dr. Angle, would it be out of order at this time to ask Dr. Judd to say a few words about preoperative preparation of the colon and his views on staphylococcus enteritis in relation to broad-spectrum antibiotics. I think you have studied this quite a bit, haven't you, Dr. Judd?

Dr. Judd: Well, I think it would depend on what day you caught me here. We were talking about the preparation as of yesterday when I left home and I told the residents that we were going to change it again. We had thought we had this staphylococcus thing pretty well whipped for the moment. We have traditionally, as the years have gone by since Dr. Bargen took over the medical gastroenterology clinic, used a combination of three factors.

For many years the first two were the most important, that is, the really vigorous purging of the patient with castor oil or with Fleet's phosphosoda or with something that really makes the bowels move. Patients complain and that's how we know we are getting good results. The second factor is real irrigations of the colon—not just ene-

mas but irrigations. (I hear one of the sisters laughing back there). We have had one of the nurses assigned at our St. Mary's Hospital and she is a good Irish nurse by the name of Connelley who has made this a real specialty. She can really irrigate these people and if we have a person we're concerned about on one of the other floors who is there for preoperative preparation we sneak around behind the scenes and try to transfer the patient up to the fourth floor where Miss Connelley is. It takes at least two days to get all this done.

Now, concomittantly with that, the third factor of the antibacterial agent has come in recent years. In the sulfasuxidine days we never had it so good, really. That's a wonderful drug. If you can take five days to use sulfasuxidine, it's great. It will not sterilize the stool but it will produce a relative sterility and reduce the colony count tremendously. At surgery when you look at the mucosa it looks just like the serosa. Everything is completely glistening and there is no sign of any normal stool present. The trouble is that it takes five days and it's not 100 per cent perfect for sterilization. It was not until the days of Chlortetracycline that we finally got a sterile stool. After two days of this drug by mouth we could take the stool from one patient and pour it over a stool colony that was growing in the laboratory and this stool would kill off the bacteria in the other patient's stool proving that it really was loaded with Chlortetracycline. The trouble is that the pH of the drug is around 1.0 and we soon found that people with peptic ulcer were bleeding and perforating and we had to quit that.

Then Oxytetracycline came along, and it seemed to be just as effective, but I secretly wondered whether that was the start of a lot of our staphylococcus troubles. We banned it from our own service for several years and used just Neomycin and that seemed to be just fine, because we achieved almost sterile stools with Neomycin alone. With the mixture of Neomycin and Oxytetracycline we can get sterile stools. But of course, the trouble is that with a sterile stool you're setting the stage for staphylococcus disease. So when that happens we get disgusted and stop the antibiotic and use just irrigations and purges. That works all right but we get into the obvious difficulty of gram-negative abscesses and wound infections and the colony count is significant enough so that we do have infections.

As you can see we blow hot and cold on this problem but Neomycin alone finally got to the point where it was giving plenty of staphylococcus trouble, too. Yesterday I told the residents we'd stop the antibiotics again. When I get home I will have several cases lined up and when we get a couple of gram-negative abscesses, I don't know what we'll do next. We'll probably go back to Neomycin.

Dr. Shultz: Dr. Judd, what do you think of the Neomycin and sulfathaladine preparation?

Dr. Judd: That is excellent, I believe. Now, I think Dr. Poth uses, what—four days of these?

Dr. Shultz: No, sir, he now advocates a rapid 24 hour preparation which we have used satisfactorily in several cases.

Dr. Judd: We haven't done many that way. It sounds good. I believe he had many years of chemical training before he went into surgery and he really knows what he's talking about. He also will put Neomycin into the peritoneal cavity which has been demonstrated to us quite conclusively to be dangerous, because there have been respiratory arrests. We talked to Poth about this, and he said the respiratory arrest is due to the curare-like agents that you're using but, be that as it may, we have not poured the drug into the peritoneal cavity, since hearing of these respiratory problems. When we have an obstructing case, where we can't take the time for preparation, we might inject this material into the proximal loop while, or immediately after, doing the anastomosis and that might help a good deal.

#### Dr. Angle:

Case #8 Record No. 22328 Mr. T. H. Age 59 Admitted 8/18/57 with a three weeks' history of abdominal cramps and borborygmi. One week prior to admission he had an acute obstructive episode and was explored by me in the Taos Hospital. A massive tumor of the transverse colon was identified and cecostomy was done for decompression. He was transferred to this hospital at which time physical examination was negative except for a 12x8x6 cm. movable mass in the left upper quadrant. He had a well-healed right rectus incision and a cecostomy with tube. Other findings essentially negative.

After a Sulfathaladine preparation on 8/21/57, he was explored through an upper transverse incision. A wide resection of transverse colon with omentum was carried out and end-to-end anastomosis performed. He had an uneventful postoperative course. Pathology revealed: Ulceration of the tumor with penetration through the bowel wall. There were 2 polyps in the distal specimen. 36 nodes examined in the tissue were all negative for carcinoma.

He was discharged 8/28/57 and returned 9/4/57 for closure of the eccostomy. On 10/9/60 he was readmitted

for small ventral hernia at the site of the cecostomy. At this time barium enema was entirely negative. On 4/19/61 after a mild vague indefinite abdominal distress of 1 week's duration barium enema revealed a filling defect in the ascending colon. Physical examination again entirely negative and after Neomycin-Sulfathaladine prep on 4/21/61 he was explored and found to have a polyp tumor in the right colon. A right hemicolectomy was carried out with an end-to-end anastomosis. Pathology revealed a 2 & ½ cm. polyp which was adenocarcinoma. All lymph nodes examined were negative. An uneventful postoperative course ensued. At the present time this patient is in good health with no sign of recurrence.

**Dr.** Angle: May we see the x-rays at this time, Dr. Friedman?

Dr. Friedman: The first film was made at the time of a barium enema three years after his operation and it shows a normal colon. The site of the anastomosis is seen and there is nothing to suggest a recurrent neoplasm. Then came the examination in April, 1961, and it's quite obvious that he now has an irregular filling defect in his mid-ascending colon which was interpreted as a new lesion (Fig. 3). That was resected as was noted and this is the examination that was made today. The anastomosis is situated at this point. Some air has been introduced in a double contrast medium and in today's examination there is nothing to suggest a local recurrence.



Figure 3

Case Number Eight. Filling defect in mid-ascending colon, site of new tumor, April, 1961.

**Dr. Angle:** Thank you, Dr. Friedman. Dr. Shultz, do you have any comment?

**Dr. Shultz:** Yes, there are several morals. First, did this man have a rather diffuse group of polyps

which became carcinomatous? At the time of the first surgery there were two adenomatous polyps in the specimen. Or, was there intraluminal spread of the one carcinoma at the time of the first resection? The usual precautions of Penrose drains' occluding the lumen, and so forth, were carried out at the time of first surgery, but intraluminal seeding was of course possible. I lean toward the polyp theory.

The second point is the absolute necessity for repeated periodic follow-up with barium enema examinations on individuals with either carcinoma of the colon or polyps of the colon. I think we were extremely fortunate that with the extent of the primary carcinoma at first surgery this man has survived without apparent metastases. He had penetration of the bowel wall with tumor at his first operation.

Dr. Judd: I think I would agree with Dr. Shultz that the time interval is such that I don't think that it was seeding from the one tumor because I think you would have known it sooner. The multiple polyp theory, I think, is very important. The finger is pointing at this particular patient. He has a colon which is a dangerous one and he may well have other tumors later. Apparently he has no polyps in the rectum by sigmoidoscopy and maybe he won't have further trouble.

If you only had a crystal ball at the first operation you could tell whether to take most of the colon out then. Of course, we don't have such an instrument but at the time we wish we did. Dr. Wangensteen might argue for an abdominal colectomy at this time on a prophylactic basis. That seems a little radical to us because the rest of the colon in the laboratory would look entirely normal, probably showing no changes of premalignant type at all, so that it would be a tremendous procedure to take on for prophylactic reasons.

It's interesting to me that when Dr. Wangensteen does do a prophylactic type of colectomy he still saves the cecum and the first part of the ascending colon and turns them down to anastomose with the lowermost sigmoid or rectosigmoid. You would think that that is still saving enough colon which would be potentially lethal and subsequently it might be difficult to put a sigmoidoscope into it and difficult to x-ray to tell whether changes are developing in the form of polyps. I don't know

what the best idea would be. I would think that we would really keep our fingers crossed for the future on this individual.

Dr. Angle: Dr. Derbyshire, do you have any comments?

Dr. Derbyshire: I want to ask one question; if this man has further trouble would you do a total colectomy?

Dr. Judd: Yes, I would. I'd do an abdominal colectomy and an ileorectosigmoidostomy.

Dr. Derbyshire: Would you have done this at the second time?

Dr. Judd: I don't think so, no.

Dr. Angle: Are there any questions from the floor?

A Physician: Would Dr. Judd comment on car-

cinoma complicating diverticulitis?

Dr. Judd: We are asked that question from time to time, and we are asked whether we do not think that the colon, with diverticulitis in it. is more prone to develop cancer. We have no proof of that. Ponka at the Henry Ford Hospital had a rather good article recently trying to indicate that this is true. Dr. Chester Guy in Chicago has tried to indicate it too, but there is no way to prove it. We do know that if a carcinoma develops distal to a pre-existing area of diverticulosis, it is easy to imagine that the obstruction produced by the carcinoma will produce secondary diverticulitis. The difficult thing to analyze is when the carcinoma develops proximal to the area of diverticulosis and there is no obstructing mechanism at all. I don't think that we are prepared to say that there is more than just coincidence at the present time.

#### New Blood Bank Program

An increasing number of inquiries by patients has prompted Southwest Blood Banks to remind the medical profession of a program designed to reduce transfusion costs and eliminate the need for replacing blood.

The program is an outgrowth of Southwest Blood Service Plan, previously offered as a service of Southwest Blood Banks, the nation's largest medically-sponsored, non-profit, self-supporting blood banking system. This service has been ruled to be an insurance program, and to continue providing protection to its members, the Blood Service Plan Insurance Company was incorporated, with Southwest acting as supervising general agent.

Although the organization is noted throughout the Southwest for blood banking service to hospitals, the insurance aspect is not so well known. The plan is designed to cover blood bank charges for whole blood, plasma, or special whole blood preparations for a small annual premium or donation of a pint of blood.

For your patients' information, details on the program are available at any Southwest Blood Bank.

# MEETINGS

# Southwest Ob-Gyn Society To Meet In Phoenix, Oct. 10-13

The twelfth annual meeting of the Southwest Obstetrical and Gynecological Society will be held in Phoenix, October 10-13, 1962, with head-quarters at the Camelback Inn.

Scheduled to address the society, which draws its membership over an area extending from West Texas to southern California, will be Dr. John Paul Stapp, Colonel in the U. S. Air Force, who is assistant to the Commander of Aerospace Medicine, Brooks Air Force Base, San Antonio, Texas. Dr. Stapp is well known for his accomplishments in the field of space medicine and specifically for his record at Holloman Air Development Center in the rocket sled program.

#### **Speakers**

Dr. Stapp will talk on "Manned Balloon Flight", "Challenge of Manned Space Flight", and "Crash Protection".

The perennial guest speaker at the society's meeting, Dr. Ralph A. Reis of Chicago, will be on hand with his ready supply of wit and knowledge. Dr. Reis is Professor of Obstetrics and Gynecology at the Northwestern University School of Medicine and Editor of Obstetrics and Gynecology.

Other guest speakers will be Dr. George H. Gardner, Chicago, Professor and Chairman of the

Department of Obstetrics and Gynecology, Northwestern University School of Medicine.

Dr. John I. Brewer, Chicago, Professor of Obstetrics and Gynecology, Northwestern University School of Medicine.

Dr. Martin L. Stone, New York, Professor and Chairman of the Department of Obstetrics and Gynecology, New York Medical College.

#### Subjects

Topics of the above three speakers will be:

Dr. Stone, "Septic Abortion with Vascular Collapse", "Precocious Puberty" and "Chemotherapy in Gynecological Malignancy".

Dr. Brewer, "Diseases of the Trophoblast", "Endometrial Carcinoma" and "Postmenopausal Bleeding".

Dr. Gardner, "The Broad Ligament—Some Interesting Observations" and "Low Backache in Women: A Gynecological Problem?".

Officers of the society are Dr. Zeph Campbell, Phoenix, president; Dr. Hobart Kelly, Riverside, Calif., president-elect; Dr. Max Costin, Tucson, vice-president; Dr. Charles T. Franklin, La Mesa, Calif., secretary: and Dr. Francis L. Rook. San Diego, treasurer.

# ORIGINAL ARTICLES

## Leiomyosarcoma of the Mediastinum

EDWARD WASSERMAN, M. D.,\* Bridgeport, Conn.

The presence of a leiomyosarcoma arising in the mediastinum is a rare finding. It is also unusual for metastases to occur. This case unexpectedly revealed a leiomyosarcoma of the mediastinum with erosion of the left side of the aortic arch producing a rupture of the aorta into the left pleural cavity. Metastatic leiomyosarcoma was found in the apex of the left lung. Because of the unusual location of this neoplasm with its subsequent erosion into the aorta, and because no similar cases have been recorded, the following report is presented.

#### Case Report

This 73-year-old retired machinist was in good health until four weeks prior to admission, at which time he noted onset of recurrent, brief "choking" sensations, unrelated to effort. At about the same time, he developed a cough productive of a small amount of yellow, nonbloody sputum, and a marked degree of hoarseness. These symptoms persisted, and one week later mild exertional dyspnea appeared and he began to vomit once or twice daily after meals. He denied abdominal pain, change in bowel habits or color of stool, chest pain, edema, anorexia or weight loss. Three weeks before hospitalization, he was digitalized and remained on 0.25 mg. of digoxin daily.

Past history revealed only that asymptomatic hypertension had been detected one year previously, for which no treatment had been given. Otherwise, review of systems and family history were noncontributory. He admitted a daily intake of at least two or three glasses of beer and one or two glasses of whisky for many years.

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Physical examination on admission revealed temperature of 98.6, respiratory rate of 20 per minute, blood pressure 180/100, and pulse of 72. The head, eyes, ears, nose and pharynx were within normal limits. The trachea appeared slightly deviated to the right. The skin revealed no spider angiomata. A firm, nontender liver edge was palpable about two finger-breadths below the right costal margin.

There was no ascites or pedal edema, but evidence of chronic varicose vein disease with stasis pigmentation was present in both legs. Pulses were present and of equal intensity in both arms and legs. Heart size was indeterminate, rhythm was regular with infrequent premature beats, there were grade 1-2 apical and basal systolic murmurs, A2 equaled P2, and no friction rubs were audible. Examination of the lungs revealed dullness with diminished breath sounds at the left base. The fundi revealed mild tortuosity of vessels without hemorrhages or exudates.

White blood cell count on admission was 5100 with a normal differential. Hemoglobin was 88 per cent or 13.7 grams and hematocrit was 44 per cent. Sedimentation rate was 36 mm. Urinalysis was negative. A fasting blood sugar was 152 mg. per cent, blood urea nitrogen 9.3, alkaline phosphatase 4.41 mg. per cent, thymol turbidity eight units, cephalin flocculation two plus, and a total serum bilirubin was 2.4 mg. per cent with a direct reaction of 1.06. A stool was guaiac positive. A VDRL slide flocculation test was reactive in whole serum but not in 1:2 dilution. A KRP complement fixation test (treponemal antigen) was non-reactive. A sputum culture produced only non-pathogenic organisms.

Thirty minutes after admission, he experienced a brief episode of "choking," which was associated for the first time with mild, non-radiating substernal pain. An electrocardiogram taken at this time showed a regular sinus rhythm with infrequent premature ventricular beats. ST segments were slightly depressed in leads 1, 2, and V4-V6. The T waves were diphasic in leads V4-V6. It was interpreted as indicating non-specific ST and T wave changes consistent with myocardial ischemia.

The patient thereafter felt well and, on the following morning, gall bladder x-rays revealed adequate function but with an unusual contour which it was thought might indicate extrinsic pressure. Several calcifications were visible above the gallbladder.

He was asymptomatic, except for the cough, on the second hospital day, when he noted the abrupt onset of severe substernal pain, described as "crushing," and associated with profuse diaphoresis and vomiting of a nonbloody mixture of food particles. Blood pressure fell to 60/50 and he was treated with 02 and aramine. The following morning his blood pressure had risen to 118/68, but he was unable to remain out of 02. Serum transaminase was 170 units and a repeat cardiogram showed inversion of the first portion of the T waves in leads 1, 2, AVL, V5-V6. Marked inversion of T waves appeared in leads 3 and AVF with a diphasic T in V3.

A bedside portable chest plate revealed total opacity of the left chest with a moderate right shift of the heart. There was blunting of the right costophrenic angle and the left cardiac border was obscured. The visible portion of the right lung field was clear. Physical examination revealed dullness with diminished breath sounds in the lower two-thirds of the left lung field. On the third hospital day, his condition remained essentially unchanged except that he began to expectorate large amounts of a bloody-tinged material and temperature rose to 101.4 degrees. Red blood cell count at this time was 2.5 million with 52 per cent (8.1 grams) hemoglobin and 26 per cent hematocrit. One unit of packed red cells was administered. On the fourth day after admission, he progressed into pulmonary edema and expired, despite vigorous treatment with tourniquets, intravenous aminophyllin, morphine, and diuretics.

#### Autopsy Findings

There was a mass located in the upper part of the mid-mediastinum, above the left main bronchus and attached to the aorta but without protusion into its lumen. The area of attachment was necrotic. At about the level of the left subclavian artery, the aorta had eroded and ruptured into the left pleural cavity which contained 1000 cc. of bloody fluid. The tumor was walnut-sized and rather hard in consistency. It was hemorrhagic and revealed whitish-yellow areas. A frozen section revealed a tumor consistent with a leiomyosarcoma. The apex of the left lung revealed a small, hard mass (1.5 cm. in diameter) of greyyellow color with hemorrhage.

Sections of the tumor found in the wall of the aorta which had ruptured showed a tumor of somewhat variable characteristics. For the most part, however, it was made up of fascicles and bundles of interlacing cells with elongated, spindle-shaped, hyperchromatic nuclei with rounded ends (Fig. 1). Mitoses were common and giant cells were noted with some regularity. Myofibrils were demonstrated with ease on special stain, but no cross-striations were visible.

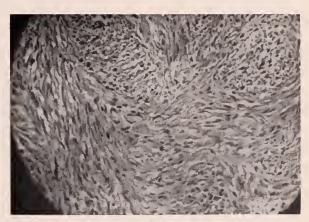


Figure 1 Leiomyosarcoma (high power).

Some sections revealed marked hyalinization of the tumor and in these areas the necrosis was most prominent, although necrosis and extensive hemorrhage were noted in many regions of the tumor. In no section was it demonstrated that the tumor arose from the wall of the aorta, although it encroached on the adventitia of the aorta in some regions (Fig. 2). The aorta itself revealed severe arteriosclerosis with marked thickening of the intima by hyalinized, fatty, and crystalline material.

The nodule in the apex of the left lung proved to be a tumor of the type described above with



Figure 2 (lower power).

Section showing aortic media on the far left. Elongated thin dark area in far left lower region is a small adventitial blood vessel. Remainder of section shows leiomyosarcoma encroaching on adventitia of the aorta.

extensive hemorrhage and cell type identical to that seen in the aorta.

In addition, there was a mild fatty degeneration of the liver with Laennec's cirrhosis, focal acute bronchopneumonia, and severe atrophic gastritis. Examination of the coronary arteries and myocardium revealed only small focal fibroses.

#### Comment

Leiomyoma is an innocent tumor of smooth muscle and is perhaps the most common tumor in the body, namely the uterine fibroid. Less commonly, it is also found in the ovaries, fallopian tubes, broad ligaments, ureters, bladder, and gastrointestinal canal where it often forms polypoid masses projecting into the lumen. Microscopically, it consists of interlacing bundles of smooth muscle fibres separated by a varying amount of fibrous tissue. Occasionally part of the tumor may become malignant and is then called a leiomyosarcoma, in which the nuclei are larger, the cells are more active-looking, and mitotic figures are visible,1 These seldom give rise to metastases, and may not recur after removal, so that they are not considered highly malignant.

Leiomyosarcoma has seldom been recorded as arising from the large blood vessels. Abell reported

two cases of leiomyosarcoma of the inferior vena cava.<sup>2</sup> In his review of the literature, he found only six tumors of smooth muscle, benign or malignant, that arose from the wall of the inferior vena cava. In another review of thirty-six cases of leiomyosarcoma of the superficial soft tissues, only one was found arising in a large vein.<sup>3</sup>

In 1960, Mariasusai and Fine reported two cases of leiomyosarcoma, one primary in the inferior vena cava and the other in the right internal jugular vein.<sup>4</sup> They also reviewed twenty-seven previously reported tumors arising in major veins. A tumor mass, pain in the area of the tumor, and symptoms secondary to obstruction of the involved vein by tumor, were the presenting complaints. Recently, there has appeared a report of a case of metastatic leiomyosarcoma involving the heart secondary to a primary tumor in the uterus.<sup>5</sup>

In the present case, it could not be demonstrated from the available sections that the mediastinal leiomyosarcoma actually arose from the wall of the aorta, although some areas revealed encroachment on its adventitia.

#### Summary

The case of an elderly male is presented who complained of recurrent choking sensations for one month prior to expiring in pulmonary edema. Autopsy unexpectedly revealed a mediastinal leiomyosarcoma encroaching upon, and eroding into, the aorta which had ruptured into the left pleural cavity. There also was the rare finding of a metastasis in the apex of the left lung. It is believed that no similar cases have previously been reported.

I am grateful for the contributions of Drs. R. B. Hill and Ozinal of the Bridgeport Hospital Pathology department.

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# Surgical Management of Vascular Lesions\* Current Concepts

George L. Jordan, Jr., M.D.\*\*

The problems of vascular surgery have long been of interest to the clinician, and valuable contributions to this field have been made periodically during the past 100 years. More than 50 years ago, for example, Alexis Carrel developed principles of suture technic which are still in use today<sup>2</sup>. He also demonstrated that defects in the arterial wall of animals could be successfully replaced with prosthetic materials3. He, as well as others, recognized that the optimum method for treating vascular lesions should be reconstitution of normal blood flow by replacement or reconstruction of the diseased segment of artery; but, until recent years, therapeutic attempts were largely limited to the aneurysmorrhaphy procedures described by Matas<sup>11</sup>, and to the occasional repair of a traumatic injury to a peripheral vessel.

The development of vascular surgery was impeded for many years by the limitation of knowledge concerning blood replacement, fluid and electrolyte shifts as well as limitations of anesthesia. As knowledge in these fields increased, direct attacks upon vascular lesions became possible. In 1952 Dubost<sup>8</sup> reported the first successful excision of an abdominal aneurysm and replacement by homograft followed shortly thereafter by the report of DeBakey and Cooley of resection of a thoracic aortic aneurysm.5 Since that time, progress has continued at a steady, rapid pace so that now the principles for surgical management of lesions of the aorta and the major peripheral vessels are well standardized and treatment is being accomplished with steadily decreasing mortality rates.

#### Aneurysms of the Aorta

The most serious common lesion involving the great vessels is aneurysm. In the past the term

aneurysm suggested syphilitic involvement of the thoracic aorta to many clinicians, but today, with the aging population and the progressive control of syphilis, aneurysms of the abdominal aorta are much more common. In fact, in a review of 903 cases of aneurysm of the aorta treated in the Baylor Affiliated Hospitals in recent years, 692 were in the abdominal aorta and 211 in the thoracic aorta4. The most serious lesions are those located in the thoracic aorta, for only 50 per cent of patients survive more than one year after diagnosis. Aneurysms in the abdominal aorta also carry a poor prognosis; 30 per cent of patients with these lesions are dead within one year and less than 20 per cent of patients survive for five years or more after diagnosis. It has repeatedly been demonstrated that the most common cause of death in patients with aneurysms is rupture of the aneurysm<sup>6</sup>.

Aneurysms of the aorta frequently cause few or no symptoms until rupture occurs or until rupture is eminent. In the thoracic aorta they are often first diagnosed by roentgenographic examination or because the patient complains of a mild chest pain. An abdominal aneurysm may be suspected by the patient when he feels a pulsating mass in his abdomen or has mild back pain. Diagnosis of abdominal aortic aneurysm is predicated primarily upon physical examination. A true pulsatile mass in the mid line of the abdomen must be considered an abdominal aneurysm until proven otherwise. Occasionally, an overlying solid lesion, such as carcinoma of the pancreas, may be mistaken for an aneurysm but the diagnosis based upon physical examination should be accurate in most instances.

Aortographic studies are rarely necessary and, in fact, may be misleading, for a thrombus may fill most of the aneurysmal sac leaving a lumen which is similar in size to the normal diameter of

<sup>\*</sup>Presented before the American College of Surgeons, New Mexico Chapter, Silver City, New Mexico. \*Associate Professor of the Cora and Webb Mading Department of Surgery, Baylor University College of Medicine, Houston.

aorta. In contrast, angiocardiography is of great value for diagnosis of aneurysm of the thoracic aorta. Although the proper diagnosis may be suspected on a simple roentgenogram of the chest and confirmed by fluoroscopic examinations demonstrating pulsation of the mass, the rapid injection of radiopaque material into an antecubital vein with proper exposure of a roentgenogram will demonstrate filling of the aneurysm with dye in most instances. Accurate diagnosis of thoracic aneurysms in this manner has become increasingly important for resection requires utilization of special technics to protect the brain, the spinal cord and the kidneys during the period of aneurysmal resection. These elaborate technics are not necessary for resection of solid tumors in this region.

The treatment of aortic ancurysms, whatever their location, is excision and replacement with a graft or prosthesis. Originally homografts were used to replace excised segments of the aorta but increasing clinical experience as well as studies in animals has demonstrated that homografts undergo retrogressive changes and may ultimately develop atherosclerosis with aneurysmal dilatation or occlusion<sup>10</sup>. Furthermore, homografts are difficult to procure and process in sufficient numbers to treat the many patients affected with these lesions in our aging population. Currently, therefore, resected segments of the aorta are replaced with a plastic prosthesis such as a knitted, crimped dacron prosthesis.

The best results in management of aneurysmal disease are obtained with aneurysms of the abdominal aorta. The mortality rate for treatment of this lesion was high in 1953, but there has been a progressive decrease so that currently the operative mortality rate is less than that following resection of the colon. There are a number of factors which affect the mortality rate. The most important is the presence or absence of rupture of the aneurysm. When the aneurysm is treated electively, the mortality rate is quite low (two per cent to three per cent), whereas, if the operation must be undertaken as an emergency in an attempt to salvage a patient who is having massive hemorrhage, the mortality rate is more than ten times this figure. Other factors which influence the risk of resection include the presence or absence of associated cardiac, cerebral or renal disease. Unless there is severe involvement of these organs, however, operation may still be accomplished with a sufficiently low risk to the patient to justify resection of the serious lesion.

The risk of treating aneurysms in the thoracic aorta is greater. In lesions of the descending thoracic aorta, for example, the surgical mortality rate is approximately 20 per cent; nevertheless, resection significantly improves the patient's prognosis.

# Occlusive Disease of the Aorta and Peripheral Arteries

The utilization of arterial reconstructive procedures has changed the picture of occlusive vascular disease as dramatically as that of the treatment of aneurysmal disease. It has now been well demonstrated that despite the fact that atherosclerosis is a generalized process, occlusions not only of the aorta but of peripheral vessels often occur in a segmental fashion so that the vessels above and below the point of occlusion are relatively normal. The most common lesions occur in the distal aorta, producing the classic Leriche syndrome, or in the iliac and femoral arteries resulting in typical intermittent claudication. As the lesions progress, ischemia of the skin with the development of ulceration and frank gangrene may occur.

The presence of occlusive disease to the lower extremities can be diagnosed quite accurately on the basis of history and physical examination, demonstrating decreased or absent pulses beyond the point of occlusion. However, for an accurate surgical attack upon the lesion, arteriographic studies are mandatory. One must demonstrate adequately patent vessels above and below the lesion if surgical attack is to be undertaken. For aortic lesions, the diagnosis can be accomplished by the injection of radiopaque material directly into the aorta. With proper timing, a single injection in this manner will allow mapping of the abdominal aorta, the iliac vessels, the femoral and popliteal vessels as well as upper segments of the anterior and posterior tibials. For patients in whom the occlusion is limited to the femoral artery, injection of dye directly into the femoral artery percutaneously under local anesthesia will suffice.

Aortographic studies were associated with a one per cent mortality rate and a significant complication rate only a few years ago. Technics now in use have largely eliminated the risk of this procedure. It is our belief that the needle puncture should be high in the abdominal aorta, above the major branches, that the injection of contrast material should be limited to no more than 30 cc at one injection, that repeat injections on the same day should not be employed, and lastly, that intravenous fluids should be administered immediately following the procedure to give adequate hydration, thereby decreasing risk of renal damage. More than 1,000 aortograms of this type have now been performed without a death.

Operability, as indicated, is predicated upon the demonstration of a localized lesion by aortography. Operation is not indicated in patients in whom a sufficiently normal vessel above the level of the lesion cannot be demonstrated or in those patients in whom the disease of the distal vessels is so severe that a satisfactory "run off" cannot be obtained.

Operative procedures which have been utilized for attack upon occlusive lesions include (1) excision and grafting, (2) bypass, (3) endarterectomy. The latter procedure is often combined with insertion of a patch to prevent constriction of the vessels. The choice of procedure will depend upon the size and location of the lesion and the experience of the surgeon. Currently most lesions are treated by the bypass method or by endarterectomy. Resection is rarely employed.

These technics have now been employed in lesions of the aorta, iliac and femoral vessels for nine years. The risk of surgery is low. The operative mortality is only .4 per cent for femoropopliteal bypass. The early and long term results of treatment of aortic lesions are very good. The early results in treatment of femoro-popliteal occlusions are also excellent, but with the passage of time, an increasing number of grafts became occluded. Because of this, there is no consensus at

present concerning the best technique of arterial reconstruction for treatment of femoro-popliteal occlusion but there is no doubt that restoration of blood flow significantly improves the prognosis for patients with this disease.

Within the past few years, interest has developed in treatment of lesions in other branches of the aorta. It is now recognized that approximately 25 per cent of patients with cerebrovascular insufficiency have occlusion of extracranial vessels causing their symptoms<sup>7,9</sup>. Some patients with hypertension may be relieved by removel of atheromatous lesion in the renal vessels, and some patients have abdominal pain and absorption difficulties resulting from atherosclerotic occlusion of the mesenteric vessels<sup>12</sup>. Accurate diagnosis is possible in each of these problems only by arteriographic studies. The re-establishment of blood flow to the affected organ can be accomplished with low risk and excellent chance of symptomatic improvement.

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1. Dupler, D.A., Greenwood, R.J., and Connell, J.T.: J.A.M.A. 174:123 (Sept. 10) 1960.

2. Hobbs, L.F.: To be published.

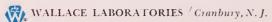
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 Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 6, Baltimore, The Williams & Wilkins Company, 1955, p. 578.

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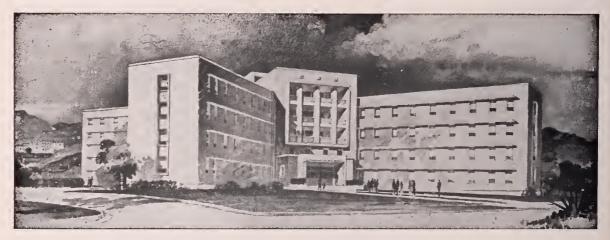
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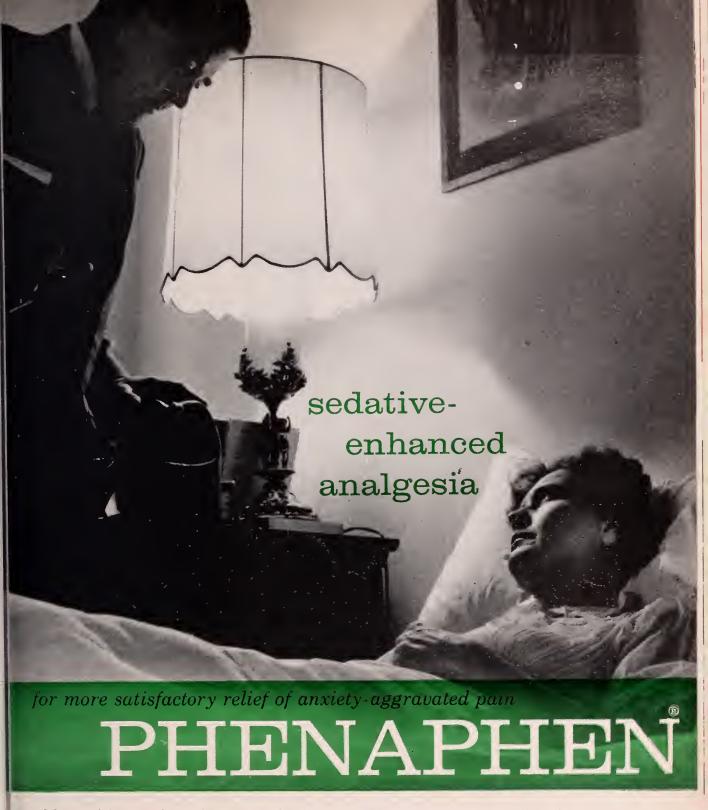
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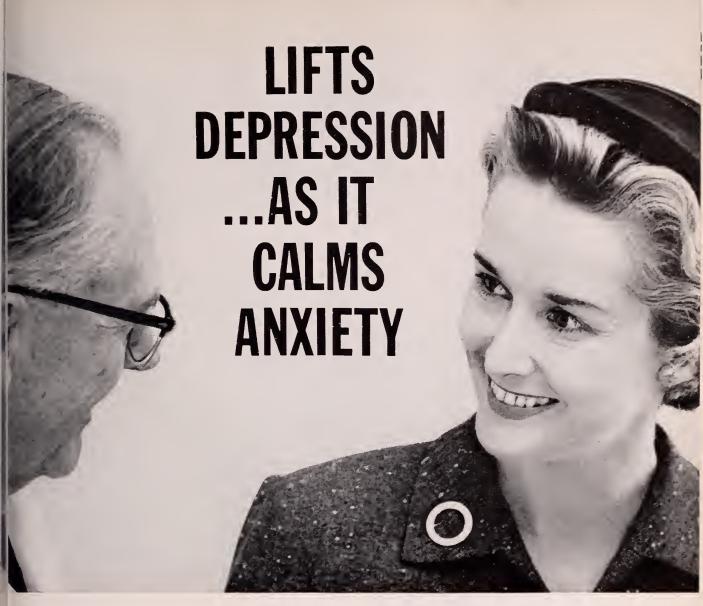
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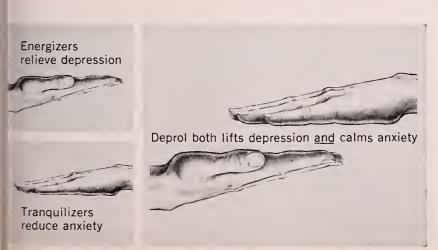
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#### Southwestern Medical Association To Meet in Albuquerque October 18-20

The 44th annual meeting of the Southwestern Medical Association will be held in Albuquerque, Oct. 18-20, 1962, with headquarters in the Western Skies Hotel.

Dr. George M. Fister, Ogden, Utah, newly elected president of the American Medical Association, will speak on "Political Placebos Via Washington" at the association's banquet on Friday evening, Oct. 19.

Other guest speakers are:

Dr. Elmer Belt, Los Angeles, Clinical Professor of Surgery at the University of California Medical Center; Dr. Thomas Findley, Augusta, Professor and Chairman of the Department of Medicine at the Medical College of Georgia; Dr. Charles A. Hunter, Seattle, Professor of Obstetrics at the University of Washington School of Medicine.

Dr. Amos R. Koontz, Baltimore, Assistant Professor of Surgery at Johns Hopkins University School of Medicine; Dr. William G. Ramer, Denver, Assistant Clinical Professor of Surgery at the University of Colorado School of Medicine; and Dr. Marcus J. Stewart, Memphis, Associate Professor of Orthopaedic Surgery at the University of Tennessee College of Medicine.

The meeting will be open and all doctors are invited to attend. Scientific sessions are scheduled during morning hours with afternoons free for recreation and sightseeing.

Dr. Harold J. Beck of Albuquerque is president of the Association. Other officers are:

Dr. M. D. Thomas, El Paso, president-elect; Dr. Frank A. Shallenberger, Jr., Tucson, vicepresident; and Dr. Grady Morrow, El Paso, secretary-treasurer.

The complete scientific program follows:

#### Thursday, October 18

9:15 a.m. Renal Diseases of Genetic Origin Dr. Thomas Findley

9:45 a.m. Surgical Treatment of Symptomatic Heart Block, and Micro-miniature Implantable Cardiac Pacemaker Dr. William G. Ranier

10:15 a.m. Coffee

10:30 a.m. Recurrent Hernia; A Perennial Prob-

Dr. Amos R. Koontz 11:00 a.m. Topic to be Announced

Dr. Elmer Belt



Dr. Belt



Dr. Findley



Dr. Hunter







Dr. Koontz

Dr. Ranier . CINCIT

Dr. Stewart

12:00 noon Luncheon and Round Table Discussion 7:00 p.m. Buffet Dinner Friday, October 19 9:10 a.m. Some Curable Types of Metabolic Bone Diseases Dr. Thomas Findley 9:40 a.m. Recent Work on Prostheses in Hernia Repair Dr. Amos R. Koontz 10:15 a.m. Coffee 10:25 a.m. Bursitis and Tendonitis; Diagnosis and Treatment Dr. Marcus J. Stewart 11:15 a.m. Common Diagnostic Procedures in Gynecology Dr. Charles A. Hunter 12:00 noon Luncheon and Round Table Discussion 6:30 p.m. Cocktails Courtesy Southwestern Surgical Supply Co., El Paso, and the Southwestern Medical Association 7:30 p.m. Banquet Presiding: Dr. Jack C. Redman, Albuquerque Guest Speaker: Dr. George M. Fister Saturday, October 20 9:10 a.m. Iron Deficiency Anemia in Pregnancy Dr. Charles A. Hunter 9:45 a.m. Management of Fractures of the

Lower One Third of the Femur

Dr. Marcus J. Stewart

Scientific Program, Dr. J. Hunt Burress, chairman; Dr. George M. Boyden, Dr. William Johns, Dr. Edwin B. Herring, Dr. William K. Woodard, and Dr. William W. Kridelbaugh. General Arrangements, Dr. Roy R. Robertson; Registration, Dr. Frank A. Rowe; Commercial Exhibits, Dr. John H. Dettweiler; and Golf, Dr. Merril W. Brown.

Mrs. Wallace E. Nissen, general chairman for the Women's Auxiliary, and her committee have planned a full schedule of activities for the ladies.

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#### Emotional Disorders in the Family Physician's Office\*

(Section One)\*\*

WILLIAM F. SHEELEY, M.D., F.A.P.A., Chief, American Psychiatric Association General Practitioner Education Project, Washington, D. C.

"... it was estimated that in Baltimore one person in eight, at a single point in time, suffered from a psychiatric disorder. Of those actually ill, about seven per cent to eight per cent are psychotic, about 15 per cent are mentally deficient, and a very small proportion, in the area of one per cent or under, are victims of acute brain syndromes. The remainder, well over 75 per cent, could be classified as psychoneurotics, character-trait disturbances, and psychophysiologic-autonomic-visceral type cases. The group of psychiatric disorders is probably as frequent and far more disabling and costly than any comparable group of diseases."

With these words, Pasamanick<sup>49</sup> uses the City of Baltimore to exemplify the great prevalence of psychiatric disturbances in the general population. He also identifies this prevalence as a medical problem involving not just psychiatrists, but all physicians. Kaplan and Milder<sup>26</sup> agree that all physicians encounter emotional disturbances among their patients when they say:

"It has been estimated that 75 to 80 per cent of all eye patients have a psychoneurotic factor in their clinical picture. Although only five to 10 per cent of these patients are truly neurotic, the overall incidence of psychoneurotic ocular symptoms is somewhat higher than in general medical practice . . ."

This prevalence of psychiatric disorder concerns all the medical profession because there just are not enough specialists in psychiatric illness to meet the needs. As Palmer<sup>47</sup> estimates, the 18,000 psychiatrists and other therapists in the country

can treat only about one per cent of the patients needing and seeking help.

#### Gate Keepers

The medical profession may be somewhat uncertain as to how to deal with this problem, but the general public is not. It looks to the family physicians. After surveying public opinion, Nunnally<sup>46</sup> says:

"General practitioners are 'gate-keepers' between the general public and psychiatry.

"First, the public views the general practitioner as the first person to contact for advice and information about mental health problems . . . second, general practitioners state that a sizable per cent of their patients are primarily troubled by 'mental' problems. Third, nearly all general practitioners are aware of psychiatric referral sources and many referrals are made. Fourth, and as important as the number of referrals, many 'mental' cases are not referred, but are treated by general practitioners themselves."

Finding examples of this public expectancy

<sup>\*</sup>Presented at the first annual New Mexico Psychiatric Seminar. Las Vegas, N. M., March 11, 1962.

<sup>\*\*</sup>To be published in two issues of Southwestern Medicine.

among their ophthalmologic practice, Kaplan and Milder <sup>26</sup> say:

"... the eye patient, speaking collectively, seems to have less insight into the possible functional nature of his complaint relative to his eyes or his vision, than is the case in other areas of medicine ... from the point of view of the patient, it makes little difference that the origin of the suffering eye may be related to some emotional conflict. He still expects that his doctor ... will take care of the pain and suffering."

Nor is the great prevalence of emotional disorders among general medical patients limited to the United States. In England, Mowbray et al<sup>43</sup> found that 15 general practitioners picked at random said about one third of their 1552 patients had significant emotional problems or components.

Furthermore, Brody<sup>4</sup> reminds us, patients often much prefer their family physician to a psychiatrist when they get psychiatric illness, Take, for example, the so-called ambulatory schizophrenic. Of him, Brody says:

"His life is sometimes punctuated by flareups of suspiciousness or aggressive excitement, but it is often flat to the point of desperation. Under these circumstances as his attention is withdrawn from external events and people, he may become preoccupied with his own body and its functions . . . (H)e eventually turns to a doctor . . . not a psychiatrist, whom he may consider as a magician or a fraud or as someone who may deprive him of his freedom—but to a 'real doctor' who can relieve him of his concern about his body and upon whom he can be comfortably dependant."

#### Family Physician

It is practical for our patients to want their family physician to deal with their emotional ills. There are many psychiatric functions which the family physician is uniquely situated and equipped to serve. Take for important example casefinding. People in emotional crisis tend to turn first to their family physician; he therefore has the first opportunity to recognize the illness, see that treatment is started, and thereby arrest the disease.

#### As Kalis et al25 say:

"The importance of seeing the patient quickly and intensively following his request for help is emphasized for at least three reasons: (1) because circumstances associated with the disruption of functioning are more easily accessible if they are recent; (2) because only active conflicts are amenable to therapeutic intervention; and (3) because disequilibrated states are more easily resolved before they have crystallized, acquired secondary gain features, or become highly maladaptive balances in and of themselves."

To back up his opinion, Kalis and his co-workers followed 40 patients first seen with acute breakdown. They found that 65 per cent recovered with only brief interviews centered around the acute crisis; 30 per cent continued in long term therapy; and only five per cent had to be hospitalized.

The family physician is also especially suited for case finding because emotional disturbances often accompany other complaints. For example, Bushnell<sup>7</sup> reminds us that:

"... when almost any ... female becomes pregnant, there are a few periods when depression of some degree becomes evident in her responses to her physiologic state. The average patient with a nonpathologic pregnancy exhibits most of her depressive episodes in the first trimester."

#### Post-Operative Care

Effgen,<sup>17</sup> remarking how often psychiatric complications seriously interfere with the post-operative care of surgical patients, says:

"I would like to suggest that whenever you suspect any kind of emotional disorder, that you are probably 99 per cent correct. Therefore, continuing on, I would like to suggest that patients be admitted for a few days 'observation' before elective surgery."

Kraft<sup>31</sup> has found that when an adolescent patient has symptoms of somatic illness, he also has fantasies about how those symptoms affect his life. Kraft therefore urges the physician gently and sympathetically to encourage the young patient to describe those fantasies so that the physician may lay to rest much unnecessary fear.

Kaplan and Milder<sup>26</sup> have found that certain symptoms of ostensible ophthalmological disease may arise from what they term "ocular neurosis." These symptoms include (paraphrased):

". . . visual disturbances which range from blurred vision to hallucinations . . . sensory disturbances including pain, itching, burning, drawing sensations and headaches—tearing, blepharospasm, retinal angiospasm, and inadequate compensation for muscle imbalances."

#### Only in Textbooks

Since pure organic or pure neurotic disorders exist only in textbooks, Mueller<sup>44</sup> says, the physician avoids the danger of ignoring organic disease because the patient is a neurotic, but he also avoids the danger of ignoring emotional disorders because the patient has organic disorders. Indeed, when a somatic disease is first beginning, and before tell-tale somatic symptoms have developed, the patient very often exhibits acute psychiatric symptoms. Furthermore, failure by the physician to see psychic disturbances in the patient's life may lead to chronic invalidism.

How then, can the physician avoid missing psychiatric disease among his patients? Laughlin, et al<sup>33</sup> answer:

"All wise physicians have known the basic importance of examining their patients in the light of their habits, dispositions, their manner of life, as well as the possible organic changes which they may have developed. Many physicians who have not had the benefit of the kind of medical education that is evolving have had to rely upon their intuition. Intuition is not an exact instrument . . ."

And Cowen<sup>11</sup> suggests:

". . . the patient is allowed to speak freely about his complaints. Encouragement should be indirect, e.g. one should not ask. 'Does the pain come on three hours after a meal; or does it come on when you are angry?' but rather, 'Exactly when and under what circumstances does the pain appear'?"

But in any case, adds Berblinger<sup>3</sup>, the physician should get answers to the following five questions:

1. Are psychiatric and medical illness simultaneously present? 2. Does psychiatric or medical illness take precedence at any given time? 3. Do psychological factors cause, precipitate, or complicate medical illness? 4. Does psychiatric symptomatology obscure medical illness? 5. Do somatic symptoms conceal the presence of a psychiatric disorder?

#### Recognize Patient

Speaking for example, of recognizing the patient with cryptic schizophrenia, Brody<sup>4</sup> says:

"The doctor's first problem is to recognize with whom he is dealing . . . evidence of unusual sensitivity, suspiciousness, hints of poorly controlled hostility, rigidly controlled thought processes, unusual elaboration of physical complaints—all of these provide clues."

(To be continued)



NEW GP OFFICERS — New officers of the New Mexico chapter of the American Academy of General Practice, elected at the annual meeting at the fifth Ruidoso Summer Clinic in Ruidoso, July 16-19, 1962, are, left to right, Dr. James A. Koch, Albuquerque, secretary-treasurer; Dr. Walter Hopkins, Lovington, president-elect; Dr. Frederick R. Brown, Roswell, president; Dr. Jack Redman, Albuquerque, retiring president; and Dr. Bram Vanderstok, Ruidoso, vice-president. Dr. Paul Feil, Deming, not in the photo, was elected a director.

#### An Aid for Interpretation of Children's Electrocardiograms

JOHN M. CASEBOLT, M. D.,

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The following group of tables and graphs is a compilation of statistics and facts from various sources, and is used in the Bernalillo County-Indian Hospital Heart Station as an aid for interpretation of pediatric electrocardiograms. It is noted that information on this subject may be drawn from (1) Zeigler's publication, which is extensive and complete, (2) several books on pediatric cardiology<sup>2,4,5</sup> from the chapter on electrocardiography, and (3) numerous journal articles on various problems within this field.

Included are notes on position; rotation; average rate for age; P wave entities; upper limits of P-R intervals for age, rate, and author; QRS complex significance, axis by age, axis distribution in cyanotic and acyanotic congenital heart disease, mean—minimum—maximum values of Q, R, and S waves in the precordial leads; criteria used by various authors for right and left ventricular hypertrophies, left and right ventricular hypertrophy patterns in systolic and diastolic overloading; T wave patterns; average and standard deviations values for the Q—T interval relative to rate; and a conversion chart for mm. to seconds.

Also included in Nadas' guide for separation and preliminary classification of congenital heart disease by the hypertrophies, and notes on patterns seen in various lesions of the cyanotic and acyanotic groups.

This paper is presented in an effort to compile a concise, handy and workable aid for interpretation of children's electrocardiograms.

#### Position

Usually vertical or semivertical up to 6 yrs.

#### Rotation

Usually clockwise up till 8 yrs, and counterclockwise after 12 yrs.

Rate (Peds Clinic of N. A.)

Age	Rate/min
Newborn	up to 200
1 mo.— 1 yr.	125—150
1 yr.— 3 yr.	115—130
3 yr.— 5 yr.	90—105
5 yr.— 8 yr.	90100
8 yr.—12 yr.	8590
12 yr.—16 yr.	80—85

mm	Rate	Sec.	mm	Rate	Sec.
1	1500	.04	39	39	1.56
2 3	750	.08	40	38	1.60
3	500	.12	41	37	1.64
4	375	.16	42	36	1.68
5	300	.20	43	35	1.72
6	250	.24	44	34	1.76
7	214	.24	45	33	1.80
8	187	.32	46	33	1.84
9	167	.36	47	32	1.88
10	150	.40	48	31	1.92
11	136	.44	49	31	1.96
12	125	.48	50	30	2.00
13	115	.52	51	30	2.04
14	107	.56	52	29	2.08
15	100	.60	53	28	2.12
16	94	.64	54	28	2.12 2.16 2.20 2.24 2.28
17	88	.68	55	27 27	2.20
18	83	.72	56	27	2.24
19	79	.76	57	26	2.28
20	75	.80	58	26	2.32
21 22	71	.84	59	25	2.36
22	68	.88	60	25	2.40 2.44
23 24	65	.92	61	25	2.44
24	63	.96	62	24	2.48 2.52
25	60	1.00	63	24	2.52
26	58	1.04	64	23	2.56
27 28	56	1.08	65	23	2.60
28	54	1.12	66	23	2.64 2.68
29	52	1.16	67	22	2.68
30	50	1.20	68	22	2.72
31	48	1.24	69	22	2.76
32	47	1.28	70	21	2.80
33	45	1.32	71	21 21 21	2.84
34	44	1.36	72	21	2.88
35	43	1.40	73	20	2.92
36	42	1.44	74	20	2.96
37	41	1.48	75	20	3.00
38	-10	1.52			

#### P Wave

Upright I, II, V4, V6, Inverted III, AVL, V1, V2

Up to age 3 voltage is 2.5 to 3.0 mm, and are peaked with a duration of 0.05—0.07 sec. Slurring of the ascending limb has no significance.

Axis Zeigler 
$$+ 75 - + 80$$
 degrees INC  $+ 60 - + 65$  degrees

"P Congenitale" Peaked with tall (3 mm or more) slightly slurred and notched, or normal duration in most cases, in I, II, AVF, AVL. In V1, V2 they are sharply diphasic with a predominant positive phase.

—Suggests right atrial enlargement (hypertrophy and/or dilitation)

—More common in horizontal hearts and cyanosis.

Biatrial Enlargement is suggested by peaked, high, and broad waves (more than 0.12 sec)

"P Mitrale" (Left atrial hypertrophy)

Flat topped P waves in I and II of normal height and prolonged duration with two notches at least 0.05 sec apart.

Dextrocardia is suggested by inverted PI and confirmed by an upright P (AVR)

#### P-R Interval

Averages 0.12 sec in the infant and 0.16 sec until 6 yrs.

#### Averages

Age	INC	Zeigler
1 mo.— 1 yr.	0.12	0.10
1 yr.— 3 yr.	0.122	0.11
3 yr.— 5 yr.	0.13	0.125
5 yr.— 8 yr.	0.132	0.134
8 yr.—12 yr.	0.14	0.139
12 yr.—16 yr.	0.146	0.149

(INC-Instituto Nacional de Cardiologia Mexico)

#### P—R Intervals for various ages and heart rates— Upper limits of normal

Age (yr.)	Below 70	71-90	91—110	111-130	over 130
0 1.5	0.16	0.15	0.15	0.14	0.13
1.5 - 6	0.17	0.17	0.16	0.15	0.14
7 — 13	0.18	0.17	0.16	0.15	0.14
14 17	0.19	0.18	0.17	0.16	0.15
small					
adult	0.20	0.19	0.18	0.17	0.16
large	0.04				
adult	0.21	0.20	0.19	0.18	0.17

#### Short

- a. nodal rhythm
- b. Wolff-Parkinson-White Syndrone
- c. Wandering pacemaker
- d. Active ectopic rhythms

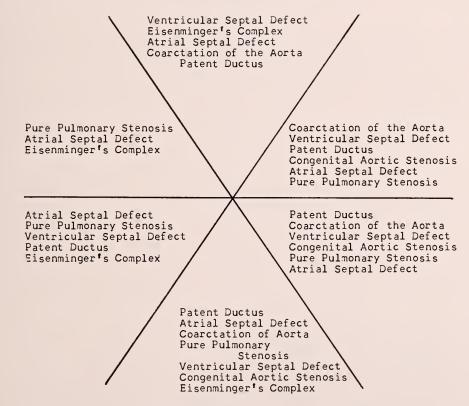
#### Prolonged—1st degree heart block

- a. congenital heart disease—ASD and VSD
- b. acute phase of RHD
- c. drug effect i.e. digitalis
- d. acute myocarditis
- e. vagotomy
- f. systemic or metabolic disturbances.

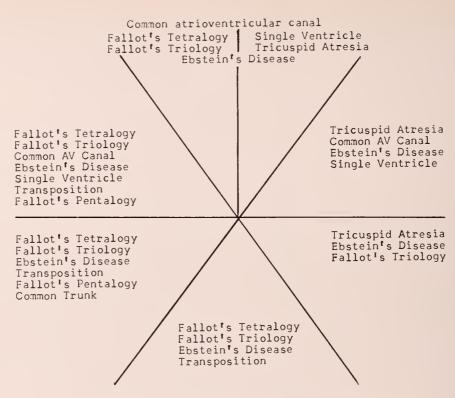
#### **QRS** Complex

- Upper limits; Infant—av. 0.06 sec. adolescent and adult—0.10 sec.
- "M" shaped, polyphasic or slurred QRS are common in children, but abnormal in adults.
- R waves are taller in children than adults.
- Q is frequently absent in I and unipolar leads during 1st week. Thereafter they should not exceed 25% of the associated R wave.

RVH pattern (normal at birth)
upright RV1, Right axis
slow transition to left ventricular pattern by
age 3-5 yrs.



Distribution of <u>acyanotic</u> congenital cardiac malformations (according to frequency). Those malformations under 0.9% incidence are not included.



Distribution of <u>cyanotic</u> congenital cardiac malformations (according to frequency). Those malformations under 0.9% incidence are not included.

	Q wave				R wave				S wave							
Age Group	V Lead	Mean				90%	Mean	Min.	Max.	10%	90%	Mean	Min.	Max.	10%	90%
0 to												4 05		0.0		10
9 mo.	V1	0	0	0	0	0	10.3	2	22	5	17	4.95	0	23	1	12
	V2	0	0	0	0	0	15.6	5	33	9	23	10.5	0.25	28	3	19
	V4	0.18	0	2.5	0	0.5	16.7	4	36	10	24	11.3	0.25	25	5.57	17
	$V_5$	0.6	0	3.5	0	2.5	13.1	2.5	28	7.5	23	5.74	1.00	15	2	10
	$\nabla 6$	0.83	0	3.5	0	2.0	9.3	0.25	24	1	16	3.12	()	11	0.5	7
10 mo.	Vl	0	0	0	0	0	8.23	0.5	26	3.5	13	6.93	0.25	25	1.5	13
	V2	0	0	0	0	()	15.3	3.0	30	8	23	14.2	0.25	28	7	23
to	V4	0.17		5	0	0.5	17.9	6.0	30	10.7	26	11.4	2.0	25	5	18
2 yr.	V <sup>4</sup>	0.17		5	0	3.0	14.6	4.0	28	8	21	4.0	0.0	15	1.5	7
	V6	1.26		5	0	2.25	10.6	2.5	24	5	15	1 6	0.0	6	0 25	3 5
9	Vl	0	0	0	0	0	6.5	0.5	20	2.5	11	9.8	1	25	3	17
3 yrs.	V2	0	0	0	0	0	12.5	3.5	25	6	19	17.3	4	33	8	27
to	V2 V4	0.12		3	0	0.5	18.3	5.5	37	10	28	11	1	34	5	17
5 yrs.	V4 V5	1.25		9	0.25	3.5	18.5	7	40	11	25	3.35	0	13.5	0.75	6.2
	$V_6$	1.28		8	0.25	2.5	13.7	4	28	8.25	5 19	1.06	0	6	0	2.5
6	3.71	0	0	0	()	()	4 9	0.5	14	2	9	10.7	1	27	4.5	18
6 yr.	Vl	0	0	0	0	0	9.7	2	21.5		14.5	19.5	6	35	11	27
to	V2	0.13		2	0	0.5	18.4	3	37	11	49	10.7	0.25	24	4	19
13 yrs.	V4			4	0.25	2.0	10. <del>1</del>	5	37	13	26	2.76	0	14	0.25	6
	V5 V6	1.0 1.04	0 ()	4	0.25		13.9	4.5	33	8.5	20	0.9	0	8	0	3

Note: 10% column indicates voltage in 10% of cases above the minimum, and 90% column indicates voltage in 90% of cases above the minimum.

Circulation 4: 420 (1951); The Unipolar Precordial and Extremity Electrocardiogram in normal Infants and Children, Mariano, Lester, Nadas, and Massell.

- The Q wave has no particular significance in pediatrics.
- RR¹ in chest leads with or without prolongation of QRS is indicative of incomplete right bundle branch block.
- If QRS is 0.10-0.12 sec. and of supraventricular origin, it is indicative of incomplete bundle branch block regardless of configuration.

Axis

Age	INC	Ziegler
1 mo.— 1 yr.	<ul> <li>75 degrees</li> </ul>	- 69 degrees
1 yr.— 3 yr.	+ 80 degrees	+ 62 degrees
3 yr.— 5 yr.	+ 69.6 degrees	+ 64 degrees
5 yr.— 8 yr.	+ 65 degrees	+ 69 degrees
8 yr.—12 yr.	+ 50 degrees	+ 64 degrees
12 yr —16 yr.	+ 73.6 degrees	+ 66 degrees

Right Ventricular Hypertrophy: not all criteria are likely to be found in any one case.

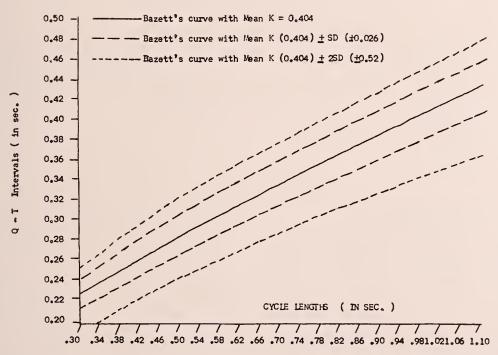
- 1. VAT V1, V2 is greater than 0.03 sec in children; is greater than 0.04 sec in adults
- 2. R V1 is prominent, Rof V3R and V4R are prominent.

- 3. RS complex of chest leads.
  - a. R-AVR is greater than 5 mm. R/S of V5
  - b. ———— ratio is less than 0.4 R/S of V1
  - c. R-V1 is 7 mm or more, and S-V1 is less than 2 mm (10 mm)
  - d. S-V5,V6 equals 7 or more mm. R-VI + S-V5 or V6 is greater than 10.5 mm. if over 5 yrs.
  - e.  $\frac{R}{S}$  (V1) is greater than 1 if over 5 yrs. is greater than 4 if 0-5 yrs.
- 4. Inversion of T in V1, V2 in adults, but this may be normal in children.

Systolic Overloading of Right Ventricle:

1. Rs, qR, qRs, rR, and R pattern with initial

Alimurung, Joseph, Craig and Massell; Circulation 1:1329, 1950



Normal Spread of Q-T and R-R Relationship. Using Bazett's formula and the mean K value derived from the data and its standard deviation, this diagram represents the normal spread of our cases. Middle curve is mean curve. Area between broken lines includes 73 per cent of the cases, and wider area between dotted lines includes 95.6 per cent of cases. (1 & 2 SD)

- slurring or notching in V1, V2. T waves may be positive or negative.
- 2. May be seen in Fallot's group, pure pulmonary stenosis, patent ductus with pulmonary hypertension, ventricular septal defect with pulmonary hypertension, Eisenminger complex.

#### Diastolic Overloading of Right Ventricle:

- 1. Diagnosis is made when right bundle branch block exists, but this may be found in normal hearts.
- 2. Most frequent in interatrial septal defect and persistent common atrio-ventricular canal.

#### Left Ventricular Hypertrophy:

- 1. VAT V5, V6 is greater than 0.04 sec in children; is greater than 0.06 sec in adults (0.05 sec by other authors)
- 2. R of V5, V6 is greater than 26 mm or 35 mm. depending on author.
- 3. ST of V5, V6 is depressed.
- 4. QRS increases beyond 0.10 sec. in adults.
- 5. R11 + R 111 is greater than 45 mm R1 + S111 is greater than 30 mm RAVL or RAVF is greater than 20 mm R of V5 or V6 + S of V1 or V2 is greater than 45 mm.

#### Systolic Overloading of Left Ventricle:

- 1. Prolonged VAT with ST depression in left ventricular leads.
- 2. Seen in aortic stenosis and systolic overloading of the left ventricle.
- 3. May also be associated with left bundle branch block and coronary disease.

#### Diastolic Overloading of Left Ventricle:

- 1. Tall R with positive, high, and peaked T waves preceded by upward R-ST displacement in V5 and V6.
- 2. Also seen in vagotonic conditons, pericarditis, hyperkalemia, etc.

T waves	V1, V2	V5, V6
0-24 hrs.	up or diphasic	down
24—72 hrs.	down	up

Inversion may be present in V3, V4, V5, V6 without indicating abnormality.

Notched T waves usually in area of T3 has no sig-

nificance.

#### Electrocardiographic Patterns Seen in Acyanotic Congenital Heart Disease:

1. Coarctation of the Aorta

Usually normal in children. In adults LVH may be present. In children RVH may be present even in congestive failure.

Nadas

#### Left Ventricular Hypertrophy or Dominance (EKG)

	NORMAL ARTERIAL SATUR		LOW AR
Diminishe		Increased	Diminished
	Coarctation of aorta Aortic stenosis Pulmonary stenosis (very mild) without R+L	Patent Ductus Aortopulmonary fenestration A ·· V Communis	Trisuspid atresi Single ventricle pulmonary steno Ebstein's diseas
	Ventricular defect (small) "Primary myocardial	Ventricular defect (moderate)	

RTERIAL SATURATION (<91%) lmonary Vasculature Normal Increased Truncus arteriosus e with Single ventricle etao

#### Right Ventricular Hypertrophy or Cominance (EKG)

	NORMAL ARTERIAL S				TERIAL SATUR	ATION (91%)
Diminished	Normal →	Increased		Diminished	Normal	Increased
Pulmonary stenosis (severe) without	Pulmonary stenosis (mild) without	Partial pulm. vein Atrial defect A ~ V Communis	anom.	Pulmonary Atria stenosis Ventr with R-L defe	icular	Total pulm, vein anom.
R→L	R+L			Transposition wi stenosis	th pulm.	Transportation without pulmonary stenosis
				Single ventricle pulmonary steno		Single ventricle without pulmonary stenosia
		Pulmonary hyper- tension with	Patent ductus	Pulmonary vascul obstruction (?p		Pulm, vascular A-V communis obstruction (secondary) defect Patent Ductus with or without coarctation Truncus arteriosus

Aortic atresia

#### 2. Congenital Aortic Stenosis

- a. P waves are biphed and notched and P11 is 0.12 sec or more.
- b. High voltage ventricular complex.
- c. Lack of axis deviation.
- d. Left bundle branch block (complete or incomplete)
- e. Inverted T waves of myocardial ischemia are common.

#### 3. Inteventricular septal defect

- a. RVH is usually present with large defects.
- Katz-Wachtel phenomenon is not as specific as originally believed. Large biphasic QRS complex in bipolar leads.
- c. Large Isodiphasic complexes in V3, V4.

#### 4. Patent Ductus

- a. Normal or LVH (Diastolic overloading)
- b. RVH rules out an uncomplicated patent ductus (systolic overloading)
- c. P waves may be slurred, notched with duration of 0.12 sec or more in bipolar leads.
- d. Large isodiphasic complexes of RS type with positive T waves in V3, V4

#### 5. Interatrial septal defect

- a. RVH is consistently found in uncomplicated defects
- b. P waves are slurred and broad in standard leads.
- c. First degree A-V block is common.
- d. Complete or incomplete right bundle branch block.
- **6.** Pulmonary stenosis with intact ventricular septum.
  - a. RVH is the rule, but may be normal.
  - T waves are usually positive in the right precordial leads unless right ventricular pressures are high, in which case the T wave becomes negative of the "ischemic" type.

#### 7. Eisenmingers Complex

- a. RVH or combined hypertrophy.
- 8. Anomalous pulmonary veins emptying into right atrium.
  - a. RVH—depending on the number of veins emptying into right atrium.

#### Electrocardiographic Patterns Seen in Cyanotic Congenital Heart Disease:

1. Tricuspid atresia with nonfunctioning right ventricle

- a. LVH and cyanosis in an infant—this is the most likely DX.
- b. P waves are broad, deeply notched and peaked in standard leads. P1, P11 usually show two peaks. PV1, PV2 are diphasic of the plus-minus type.
- c. Left axis deviation, and sometimes incomplete left bundle branch block.
- 2. Peristent common atrioventricular canal (AV comminus)
  - a. signs of RVH
  - b. signs of LVH
  - c. Right bundle branch block with left axis deviation is common.

#### 3. Ebstein's disease

- a. If sinus rhythm P is tall and peaked with slight slurring of both limbs. Also seen in right atrial leads.
  - If P waves are broad concomitant left atrial disease is suggested.
- b. Frequent arrhythmias are atrial fibrillation and flutter, premature atrial and ventricular beats, and paroxysmal atrial tachycardia.
- c. Wolff-Parkinson-White syndrone Type B is suggestive.
- d. First degree AV block is common.
- e. Right bundle branch block in precordials and AVR lead.

#### 4. Tetralogy of Fallot

- 1 infundibular and valvular pulmonary stenosis
- 2 dextroposition of aorta
- 3 ventricular septal defect
- 4 right ventricular hypertrophy
- a. RVH in almost every case.
- b. LVH or normal should be viewed with suspicion. (Tetralogy plus Patent Ductus may show LVH)
- c. "P congenitale"
- d. T wave in V1 is usually positive as well as the rest of the precordials (Distinguished from Triology of Fallot)

#### 5. Triology of Fallot

1 pulmonic stenosis-predominantly valvular

- 2 interatrial septal defect
- 3 right ventricular hypertrophy
- a. "P congenitale"
- b. RVH in almost every case
- c. Negative T waves of the "Ischemic" type in the right precordials
- 6. Transposition of Great Vessels
  - a. RVH is almost always present
  - b. Negative T waves in the left precordials
  - c. contributory signs:
    - —When T waves are higher on the right than on the left precordials
    - --Normal positive T waves in V1 and V2 and flat T waves in V5, V6
    - -Notched T waves in left precordials
- 7. Truncus Arteriosis
  - a. Usually RVH when uncomplicated
  - b. Complex of qRS or qRs type in V5, V6 are of lower voltage than in VSD or AV com-

#### minus

- c. R is high in all precordial leads
- d. T may be positive in all precordials (V2-V6) but may be negative in several
- e. Usually have high peaked and symmetrical T in 1, II, V5, and V6
- 8. Single Ventricle
  - a. Left axis deviation
  - b. P waves are normal or with minor changes in the standard leads
  - c. Same rS or RS pattern in all precordial leads

#### Bibliography

- (1) A. H. A. Electrocardiographic Test Book, American Heart Association 1956
- (2) Congenital Heart Disease, Kaplan and Robinson, McGraw-Hill 1954
- (3) Circulation 4 420 (1951), The Unipolar Precordial and Extremity Electrocardiograms in Normal Infants and Children, Nadas et al.
- (4) Pediatric Cardiology, Nadas, W. B. Saunders Co. 1957
- (5) Pediatric Clinics of North America, Nov., 1958; Electrocardiography in Infants and Children, Sodi-Pollares et al.
- (6) Ziegler; Electrocardiographic Studies in Normal Infant's and Children, C. Thomas, 1951.

#### Coming Meetings

Scott and White Clinic, Second Educational Afternoon, Temple, Texas, Sept. 15, 1962.

The Western Association of Railway Surgeons, annual meeting, Stockmen's Motor Hotel, Elko, Nev., Sept. 27-29, 1962.

Southwest Obstetrical and Gynecological Society, 12th Annual Meeitng, Camelback Inn, Phoenix, Oct. 10-13, 1962.

Eleventh Annual Conference, Health Services Advisory Committee, United States Civil Defense Council, James White Memorial Auditorium, Knoxville, Tenn., Oct. 15-19, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.

Southwestern Dermatological Society, Annual Meeting, Western Skies Hotel, Albuquerque, October 21, 22, 1962.

American Cancer Society, 1962 scientific session, Biltmore Hotel, New York, Oct. 22, 23, 1962.

#### Lectureship in Medicine To Be Held Sept. 29

"Congenital Heart Disease" is the subject of the third annual Methodist Hospital Lectureship in Medicine to be held in Lubbock, Texas, Saturday, September 29, 1962. Sessions will begin at 8 a.m. in the main ballroom of the Pioneer Hotel.

Speakers are Dr. S. Gilbert Blount, Jr., of Denver and Dr. Frank Dammann of Charlottesville, Va. The lectureship is open and all physicians in the area are invited to attend.

Entertainment includes a football game between the University of Texas and Texas Tech teams, scheduled to begin at 8 p.m. on Saturday.

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#### Methocarbamol in the Treatment of Tetanus in a Child

RIDER STOCKDALE, M.D., Jasper, Texas

Despite numerous admonitions concerning the lack of tetanus immunization, relative apathy on this subject by public and physician alike portend the continued occurrence of occasional cases of tetanus. That tetanus is not the unique property of rural areas or of low socio-economic groups has been recently discussed by Botticelli. In spite of many therapeutic advancements offered during the past few years, tetanus remains a disease with an alarmingly high case fatality rate. Several factors have been cited which offer some prognostic information (incubation periods, onset time, concommitant clinical conditions), but these are of little therapeutic benefit to the individual patient who may die as a result of this infectious disease.

Not only has the annual number of reported cases of tetanus in the United States remained relatively stable over the past 10 years (around 450), but the annual number of reported deaths from tetanus has shown little change during this period (around 250 to 300). Certainly, assuming reporting has been reasonably complete, one can gain little statistical support for a belief that our recent advancements have paid off in more recoveries from this preventable disease. Obviously, further improvement is indicated both in our preventive efforts and in our therapeutic practices.

Several articles have recently appeared in the medical literature which review the principles to be followed in the management of acute tetanus. Some of these indicate author preference for intramuscular meprobamate as a muscle relaxant in the tetanus case, and cite objections to available intravenous preparations (technical difficulty in finding veins, need for additional drugs for sedation).<sup>2,3,4,5</sup> On the other hand, others refer to the advantages of methocarbamol which can be given intravenously (avoidance of multiple needle stimulation by insertion of drug into IV tubing, better control of dose response).<sup>6,7,8,9,10</sup>

Thus, it seems worthwhile to report on a case of clinical tetanus treated successfully and uneventfully with methocarbamol\*. Further, only

one author has referred to the use of this drug in children.<sup>7</sup>

Since it now appears that the dosage required to adequately control tetanic spasms is considerably greater than that recommended for other indications, the effective dose in children likewise deserves documentation.

#### Clinical Case

A 12 year old white boy weighing 72½ pounds was admitted to the hospital December 4, 1960, with a chief complaint of "locked jaws and tightness of all muscles" of one day's duration. A history was elicited from the parents that the boy had cut his ankle on about November 27, 1960, on a dried out deer head, which had been laying in the yard of his country home for several weeks. The wound was considered trivial by the boy's mother who applied hydrogen peroxide and a dressing. He remained asymptomatic until seven days later when he noted "locked jaws." There was no history of tetanus toxoid immunization.

On examination, the masticatory muscles were very spastic and the jaws were clenched. Blood pressure was 104/70, temperature 98.8°, respiration 20 and pulse 80. Examination produced intense painful spasms of the extremities. A crusted ½-cm. wound over the left medial malleolus was observed. A diagnosis of tetanus was made and immediate treatment instituted.

Nembutal (90 mg.) was administered intramuscularly for sedation. Following an I. M. injection of 50 mg. of Benadryl, 90,000 units of tetanus antitoxin were given by the same route and an additional 10,000 units injected into the periphery of the wound. Parenteral antibiotics of the mycin group were administered as the boy was allergic to penicillin. Debridement of the ankle wound yielded a 5 mm. by 2 mm. piece of deer antler. Because of inadequate laboratory facilities, cultures were not attempted.

Following admission, the patient became progressively more spastic and restless. He was opisthotonic and generally rigid. Sedation consisting of a dark quiet room, intravenous Nembutal

<sup>\*</sup>Brand named Robaxin by A. H. Robins Co., Inc.

in doses of 45 to 90 mg. every four hours, occasional intravenous injections of promazine in doses of 25 to 75 mg., and rare doses of 50 mg. of meperidine for severe pain were used. On the first day an attempt at oral medication was followed by a severe episode of laryngospasm, dysphagia, and generalized convulsions. No further attempts at oral medication were made during the first eight days of hospitalization.

Initially the violent muscle spasms were partially controlled by one gram of injectable methocarbamol every six hours administered through the tubing of intravenous infusions. On the fourth hospital day, this dosage was increased to two grams every six hours, resulting in a definite reduction in the frequency and severity of muscle spasms and convulsions. Although necessary equipment was kept at the bedside, a tracheotomy was not performed. By the ninth hospital day the patient was able to swallow, and 1.5 grams of methocarbamol commenced every three hours by mouth in lieu of intravenous medication.

Steady improvement followed and he was discharged on the 19th hospital day. Methocarbamol (four grams daily) was continued for an additional week. A "tip-toe" gait persisted for two weeks after hospital discharge.

#### Comment

Of interest was the development of a dirty brownish-green color of the patient's urine during treatment with intravenous methocarbamol. Repeated urinalyses were negative for albumin, bilirubin, urobilinogen, red blood cells and casts. The urine was acid and the specific gravity remained between 1.010 and 1.020. The unusual urine color, thought to be due to one of the metabolites of methocarbamol and of no clinical significance, has been occasionally reported by other physicians using this drug.

Many articles have appeared in the literature concerning the various clinical aspects and efficacy of methocarbamol in various conditions. However, reports on its use in the management of tetanus have been of fairly recent origin. Although the drug can be administered intramuscularly, it is the opinion that its intravenous availability makes it a particularly desirable muscle relaxant in the management of acute tetanus cases. Not only is it remarkably effective, but it can be administered while avoiding needless and unneces-

sary stimulation of the patient by giving it through intravenous tubing. The intravenous use of methocarbamol is contraindicated in the presence of known or suspected renal pathology because of the presence of polyethylene glycol-300 in the vehicle. However, the margin of safety appears to be wide and, of course, any hazard must be weighed against the risks of uncontrolled tetanic muscle spasm.

#### Summary

Methocarbamol was used advantageously in a 12 year old patient with tetanus. In relatively large doses intravenously the drug was extremely useful in the management of the severe muscle spasm and convulsions during the acute phase of the illness. No toxic or untoward effects were observed.

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#### Nation's Oldest Essay Contest

The Trustees of America's oldest medical essay competition — the Caleb Fiske Prize of the Rhode Island Medical Society - have announced two subjects for this year's dissertation, open to any Doctor of Medicine in the nation, for which a cash prize of \$500 will be awarded.

The subjects chosen are "Etiological Factors in the Development of Congenital Anomalies," and "Progress in the Relief of Hearing Defects."

An entry on either subject must be typewritten, double-spaced, and should not exceed 10,000 words. Essays must be submitted by December 11, 1962, to the Secretary, Fiske Fund, Rhode Island Medical Society, 106 Francis Street, Providence 3, Rhode Island.

#### Britain's Medical System Described by M.D.'s Wife

(EDITOR'S NOTE—The following letter is presented here because of its bearings on the King-Anderson medical bill.)

Sirs: — In view of all the discussion of the past few weeks, I feel obligated to sit down and add my own thoughts on the subject of socialized medicine, and socialism in general.

First of all, let me make it quite plain that I am the wife of an M.D. Secondly, let me make it equally plain that I have had the dubious experience of having lived under "socialized medicine" in England; and indeed, still have part of my family living under both it and nationalized railways and other things.

I can well remember studying the proposed Beveridge Plan while in college in England. It seemed like the ideal answer to the prayers of many financially strapped British subjects—people whose burdens had been doubled by the disasters of war. One of our first questions was "Who's to foot the cost?" The answer to that question, naturally, was "The Government." That sounded all very well and good, but when you come down to it, where does the government get its money? From the people, of course. That meant higher taxes, and we felt sure that with the British tax structure as it was, people simply would not be interested in anything that involved higher taxes. They were high enough! But, as you know, socialized medicine came into being, in the form of the National Health Services. It is also interesting to note at this time that nationalized railroads, nationalized steel mills, etc., followed shortly thereafter.

I feel that many people have a tendency to go around debating issues in such generalities, that it makes it difficult for anyone interested in finding facts and figures to base their own decisions. The time has come for all Americans to decide just which way our country is going to go.

In the 'Health Services of Britain' pamphlet, published by Her Majesty's Government, we find that through the Family Doctor Service, the professional attention of a family doctor is made available to everyone. Patients may choose the doctor they wish, provided only that he is enrolled

in the Family Doctor Service Plan, and that he consents to attend them! They may also change their doctor with a minimum of formality. The doctor has a similar freedom to accept or refuse patients as he wishes. His enrollment in the service does not preclude him from attending paving patients who have not joined the service, if he cares to do so. The doctor in the Family Service is free to treat his patients exactly as the family doctor treated them in the past. There are no regulations as to what drugs or prescriptions he may prescribe, although the Chief Medical Officer of the Ministry of Health has asked doctors to consider before prescribing any propietary preparations where a standard drug or combination of drugs can be prescribed with equal effect.

This all sounds very good, but let me tell you what a number of years under this system has resulted in.

The National Health Service, which started its mission in life to give "free" medical care to the people, made what seemed a perfectly reasonable estimate of its cost to the Government. As time went along and the plan went into effect it was found that the original planned cost was grossly underestimated. This error was mostly ascribed to the abuse of medical facilities by people who just could not resist the temptation to spend their lives in doctor's offices and hospitals. There was also an enormous juggling of prescriptions for cosmetics, eye glasses, shampoos and other things sold in drug stores. In other words, if you knew how to do it-you could get almost anything for 'free," if somewhat dishonestly. As soon as this was brought to light, the National Health Service started charging, in 1952, for prescriptions.

Hospitals, in which all of us are interested, either because we have already been patients, or are afraid we are going to be patients, are an interesting side of the National Health Services Plan. British patients find it most difficult to get into a hospital—no matter how acute their illnesses may be. This is because of overcrowded

conditions in the hospitals—a condition brought on by prolonged hospitalization of chronic cases that originally were either cared for in their homes by their families or in the nursing homes. The tremendous cost of the service has precluded the government's building of hospitals since the end of World War II. So, the crowded conditions continue. Obstetrical cases can be admitted into the hospitals only if there is available bed space, otherwise deliveries take place at home or in maternity homes (also grossly overcrowded), and a doctor's presence to National Health Members is dictated by need. If a birth is normal a mid-wife officiates at the delivery. If the birth is not normal a doctor's presence is indicated. And, take note, Mothers—anesthetics such as Trilene may not be administered without the presence of a doctor or a registered nurse!

#### Abuses and Errors

In June of 1952, due to abuses and errors in calculation the Health Service was forced to initiate charges for prescriptions, dressings, prosthetic appliances and other such things to both in-patients and out-patients. So, as I'm sure is quite an obvious fact by now, patients not only had higher taxes or National Health Insurance, they had added hospital and medical costs to top it off.

Dental Service patients are provided with all forms of treatment for restoration of dental fitness. As in the family Doctor Service, the patient is given complete freedom of choice of dentists and the dentist is given free choice of patients. All conservative dental treatment (eg. fillings), extractions for relief of pain and ordinary denture repairs may be given without reference to outside authority; but, extensive work (eg. prolonged treatment of gums, gold fillings, in-lays, denture crowns and special appliances and dental surgery) may be given only with authority of the Dental Estimates Board. In May, 1951, charges were introduced for dentures, whereby the patient has to pay a little under half the total cost. In June, 1952, a charge of one pound (somewhere around \$3 U. S. at that time) or the full total cost of any treatment if less than one pound was introduced.

Doctors and dentists and other medical personnel are not poorly paid, as is so often thought. They are even paid to go in practice in so called "undesirable areas." The paramount objection

doctors have is the time taken out from practicing medicine for filling out the endless forms required for each patient. The loss of the normal doctorpatient relationship, so uniquely a thing of our own, by the introduction of a third party into the practice of medicine (the government) and the fact that all the Health Service Plan has managed to accomplish in Britain is to provide more medicine to more people at a higher cost and lower quality. There is also the resultant crushing of individual initiative in both work and research: both of which we heartily respect in the United States. Then last, but not least, there is the dreadful impersonality generated by a scheme of this magnitude to be reckoned with. The population of the United States is peculiarly individualistic, and none of us will readily accept the loss of our identities for a number on a cog in a mass of grinding government machinery.

#### Fine Medical Care in U.S.

May I add that my husband and I were extremely grateful all through this past year for the fine medical care that the United States offered us. My relatives in Europe made it quite clear that had we been there during my husband's illness he would never have had the chances and the care that he had here. I am thankful for the privilege of living in the United States, and for that reason feel obligated to 'speak up' for our democratic way of life. Our country was founded on idealism and self reliance. Let us not give away our self reliance for so called security. Let us keep our idealism a tempered and realistic gift to be used wisely, not radically. Of course our form of government is not perfect—there are many things that could be improved—just as there is in medicine or any other facet of our work and lives. But let us not move too rapidly. Our country has accomplished in just a few hundred years what it has taken other countries thousands of years to accomplish. Wherever the human factor is encountered there are bound to be mistakes and abuse, but let us try to correct our errors and proceed with great thought and caution. These mistakes are easy to make but extremely difficult to un-make. The British have tried to denationalize a lot of the endeavors they so jubilantly nationalized after World War II, but it is a process that will take years and much patience.

> Mrs. Gerald A. Słusser Artesia, N. M.

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1. Hodges, F. T.: *GP* 14:86, Nov., 1956. 2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

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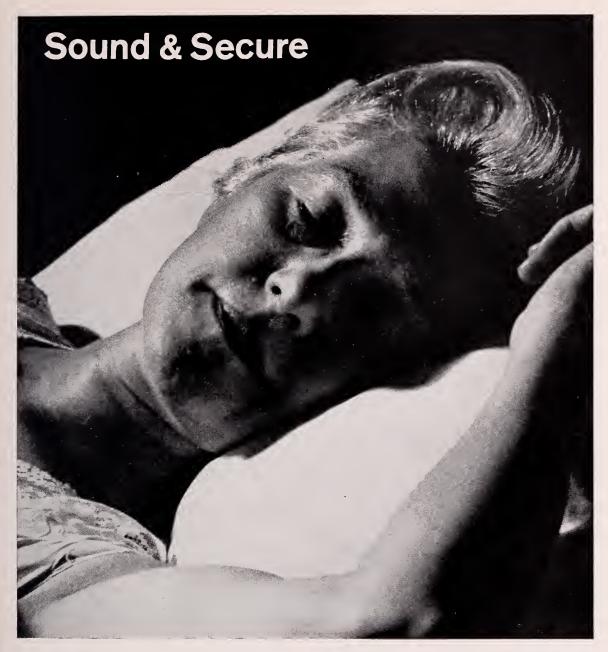
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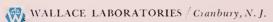
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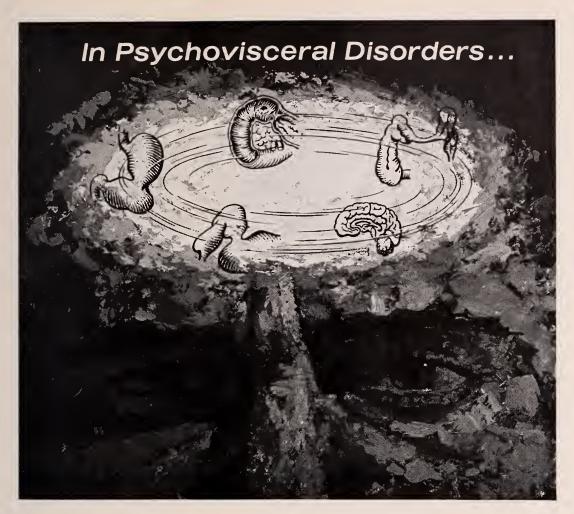
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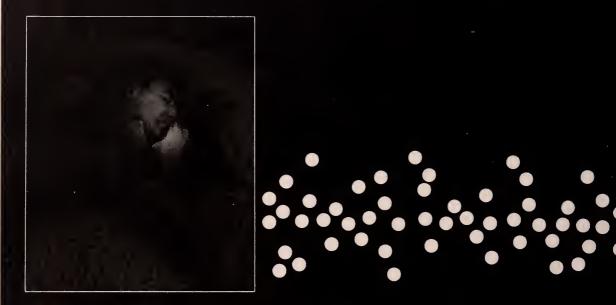
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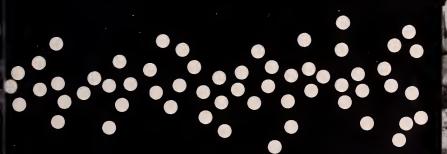
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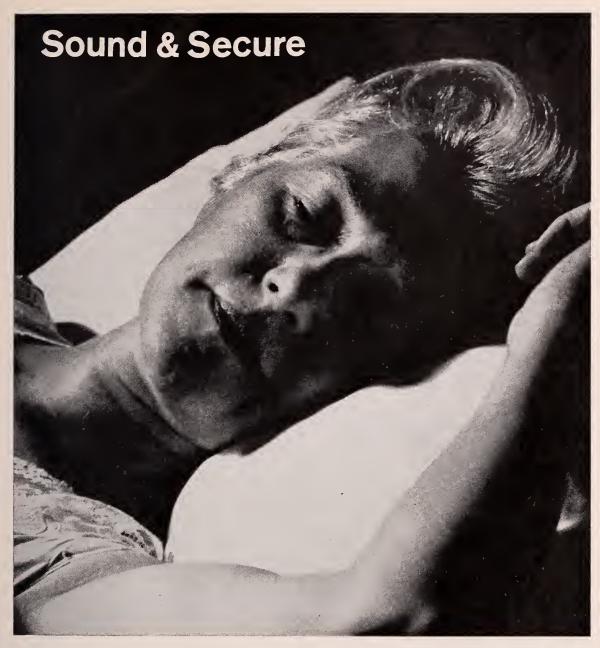
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Mysteclin-F contains Squibb Phosphate - Potentiated Tetracycline (Sumycin), plus Amphotericin B (Fungizone). Available as: Mysteclin-F Capsules (250 mg.) 50 mg.); Mysteclin-F Half Strength Capsules (125 mg./25 mg.); NEW Mysteclin-F Syrup (125 mg./25 mg. per 5 cc.); Mysteclin-F for Syrup (125 mg./25 mg. per 5 cc.); Mysteclin-F for Aqueous Drops (100 mg./20 mg. per cc.). For full information, see your Squibb Product Reference or Product Brief.

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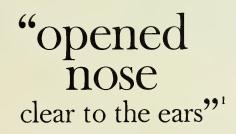
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NEW DIMETAPP ELIXIR one-third the D metapp Extentabs' formula in each 5 cc.), for conventional t.i.d or q i.d. disage in a palatable, grapulavored vehicle.

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The illustration: To dramatize the pain and trauma and healing of the peptic ulcer, our photographer burned a "lesion" into crumpled metal with a blowtorch and photographed it, then repaired the damage and rephotographed the result — the "healed" ulcer.

# ulcer under repair

"What results can I expect in my ulcer patients?" Shown below is a tabulation of 795 ulcer patients, reported by 69 investigating physicians, in which glycopyrrolate was the anticholinergic employed. They represent a cross section of ulcer patients of all ages, both ambulatory and hospitalized, under various regimens, from all sections of the country.

Note the pattern of results. Robinul showed an "excellent" or "good" response in over 83% of patients, and Robinul-PH provided similar results in 81%.

As for side effects, these often troublesome extensions of anticholinergic action such as dry mouth, blurred vision, etc., were evaluated as

"moderate-to-severe" in only 6.7% of a total of 1705 patients in preliminary investigative studies, 795 of whom are the ulcer cases tabulated here.

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Each tablet contains glycopyrrolate, 1.0 mg.; and phenobarbital ( $\frac{1}{4}$  gr.), 16.2 mg.

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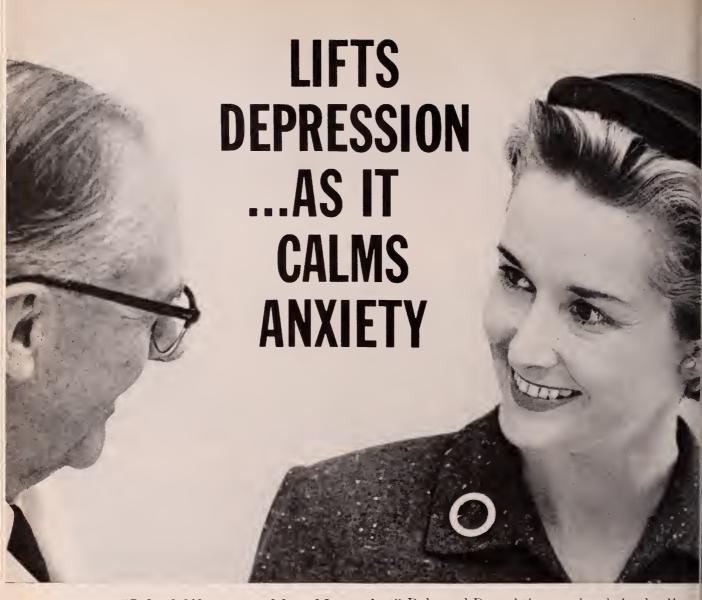
results with Robinul and Robinul-PH in 795 ulcer patients, from 69 clinical investigators\*

DIAGNOSIS	ROBINUL				ROBINUL-PH					
	*No. Patients	Excellent	Good	Fair	Poor	*No. Patients	Excellent	Good	Fair	Poor
Marginal Ulcer	11	3	3	3	2	1	0	1	0	0
Pyloric Channel Ulcer	6	3	1	0	2	2	1	1	0	0
Pyloric Ulcer	4	2	1	1	0	1	1	0	0	0
Gastric Ulcer, bleeding	3	1	2	0	0					
Gastric Ulcer	48	31	11	1	5	12	5	7	0	0
Gastric Ulcer, penetrated	1	0	1	0	0	1	1	0	0	0
Gastric Ulcers, multiple	1	1	0	0	0					
Duodenal Ulcer	494	220	195	48	31	99	41	38	13	7
Duodenal Ulcer, bleeding	38	19	15	3	1	2	1	0	1	0
Duodenal Ulcer, obstruction	13	4	3	1	5					
Duodenal Ulcer, perforated	5	2	1	0	2	6	0	3	1	2
Gastric and Duodenal Ulcer	4	2	2	0	0					
Peptic Ulcer, unspecified	25	19	4	0	2	18	8	7	2	1
TOTALS	653	307	239	57	50	142	58	57	17	10
	83.6%					81.0%				

\*Clinical reports on file, A. H. Robins Company, Inc.

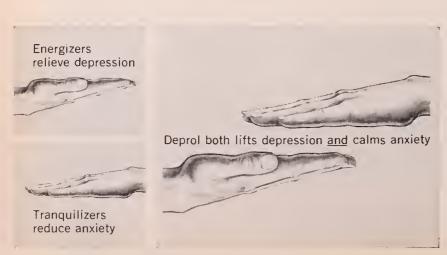
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### Coming Meetings

Southwest Obstetrical and Gynecological Society, 12th Annual Meeting. Camelback Inn, Phoenix, Oct. 10-13, 1962.

Eleventh Annual Conference, Health Services Advisory Committee, United States Civil Defense Council, James White Memorial Auditorium, Knoxville, Tenn., Oct. 15-19, 1962.

Southwestern Medical Association, 44th Annual Meeting, Western Skies Hotel, Albuquerque, Oct. 18-20, 1962.

Southwestern Dermatological Society, Annual Meeting, Western Skies Hotel, Albuquerque, October 21, 22, 1962.

American Cancer Society, 1962 scientific session, Biltmore Hotel, New York, Oct. 22, 23, 1962.

Southern Medical Association, annual meeting, Fontainebleau Hotel, Miami Beach, Nov. 12-15, 1962.

New Mexico Chapter, AAGP, Ruidoso Summer Clinic, Ruidoso, N. M., July 15-18, 1963.

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CIBBA SUMMIT, N. J.

### Surgical Treatment Of Pulmonary Tuberculosis

R. G. McCorkle, M.D., F.A.C.S., Austin

In the past decade, the surgical treatment of pulmonary tuberculosis has changed rapidly. During this period, the surgical management of pulmonary tuberculosis has been stabilized, as to indication of surgical intervention.

Most changes have been attributed to the discovery of several anti-tuberculosis drugs. Streptomycin, para-aminosalicylic acid, and isoniazid, which can be given over a long period of time, have maintained a record of satisfactory therapeutic results with fewer patients developing resistance or toxic reactions. With these drugs, we have been able to offer intensive medical treatment to patients with recurrent, chronic, or incurable tuberculous lesions.

Minimal lesions treated with para-aminosalicylic acid, isoniazid, or streptomycin, show a cure rate of 75-80 per cent within six months, and therapy continued with out-patients for another six to eight months has produced total inactivity of lesions under present regimes. Only 15-18 per cent showed therapy failure, gauged radiographically by spread or failure of resolution. About one-third or less of the total are readmissions to sanatoria, as moderately advanced or far advanced cases for repeat therapy with combinations with other antituberculous drugs.

Another significant advance has been the rapidly changing concept of surgical indications in therapy of the tuberculosis patient. Anesthetic techniques and improved surgical methods have contributed considerably to the progress of surgical therapy in pulmonary tuberculosis. The approach to the problem of treatment in generalized terms is to consider diagnosis and therapy together.

The diagnosis of pulmonary tuberculosis is usually made clinically, and on chest radiography. The symptoms of tuberculosis are well known, and the physical findings vary according to the degree of pulmonary involvement. Confirmation of diagnosis by bacteriological examination of either sputum or gastric contents is necessary. Pulmonary tuberculosis in the asymptomatic person can usually be discovered on routine x-ray survey.

#### Present Trends

Medical management is instituted once the diagnosis of tuberculosis is established. As there are many different concepts in medical therapy, for uniformity, we should consider the present trends in treatment.

First, confining all patients to complete bed rest is considered less important than it once was, but it is still essential for moderate or far advanced cases. Clinical toxicity is necessarily treated by bed rest, sanitorium care, drugs, and frequently surgery. However, there is more free-

dom of patient activity in today's program of management in early, minimal lesions.

Second, use of temporary collapse procedures, such as pneumothorax, pneumoperitoneum, and phrenic crush are considered obsolete (if not completely avoided in the medical management.)

Third, surgical procedures which reduce pulmonary function, namely thoracoplasty, are occasionally but less frequently used.

And fourth, reasonably early excision of tuberculosis residuals has been gradually discarded for an increase in medical management of from six to eight months up to 12 to 14 months and even longer.

Drug therapy of isoniazid is given in dosages of 400 to 600 mg. per day; para-aminosalicylic acid, 9 to 12 grams per day; streptomycin, one gram twice weekly. Drug resistant studies are more frequently used and are routine in patients on the therapy over four months with positive bacteriology, without radiographic improvement, and in those with definite clinical evidence of extension of disease.

### Recognition of Benefits

The most important single factor in the treatment of pulmonary tuberculosis is recognition of maximum benefits of medical treatment determined by radiological and laboratory studies, and the indications for surgical intervention. Patients with minimal lesions which have consolidated under medical therapy and show evidence of cavitation by tomograms should be resected at the end of nine months of medical therapy or sooner. This fact is somewhat in dispute, and these patients are classed as "open, negative, lesions arrested". Some of these cases have been followed for a year or more without relapse, as determined either by x-ray or laboratory study; however, it is considered wise to resect these at the end of 10 to 12 months in dispute, as a 15-22 per cent relapse is possible.

For those with more area involvement and considerable destruction of parenchymal tissue, it is important to have the lesion stabilized before resection. The morbidity and mortality is definitely increased by resection in patients who have positive drug resistant organisms present three or more months before a planned resection. Pre-

sent indications for surgical treatment of pulmonary tuberculosis have varied, but the following are general accepted indications:

- 1. Bronchial stenosis secondary to tuberculosis bronchitis. The anatomical location of the tuberculous involvement as related to primary or secondary bronchi should determine the extent of resection.
- 2. Bronchiectasis secondary to tuberculosis with symptoms either with or without abscess or cavity formation, active or inactive, symptomatic.
- 3. Lower lobe cavities, which are usually confined to dorsal segment divisions and are not very common, but require resection rather than collapse procedure.
- 4. Thoracoplasty failures are being seen less because this procedure has almost been abandoned. Resection is indicated in these particular instances.
- 5. Tuberculomas: Excision of these is questionable, except in cases of possible malignancy. The policy at present is of definite diagnosis and delay of resection. This applies to caseous nodules with or without positive sputum that persist after five to seven months of therapy. If such condition exists, continuation of medical therapy is advised. My own opinion is that tomograms should be done to determine cavitation and those cases with caseous foci should be resected.
- 6. Destroyed lobes or lungs, when suppurant, indicate resection. Such lobes or lungs actually are sources of potentially active organisms.
- Open cavities with negative bacteriology have been deferred for resection and drugs continued indefinitely, in some instances for two to three years without surgical therapy.
- 8. BP Fistulas, secondary to tuberculosis, require thoracoplasty. Resection is usually a secondary procedure, if performed at all.
- Resistant cavitary lesions with positive bacteriology should be treated first with thoracoplasty. Most cavities under 4 cm. in

diameter are not to be resected, and medical therapy should be continued until bacteriology is negative.

Medical failures are those cases which have not responded to adequate therapy of anatomical extent of disease, drug resistant organisms, or inappropriate selection of antituberculosis drugs. Extensive lung disease is seen less frequently because of continued good results with medical therapy, early resection or thoracoplasty. However, there is an increase in mortality of patients with positive sputum who have undergone resection. The mortality increase is about five per cent in these patients. Fewer thoracoplasties are now done in conjunction with pulmonary resection, and, if done are performed usually late in the postoperative period.

Pneumoperitoneum is used in the postoperative period to reduce residual air cavities in patients whose air pockets are less than 200 cc.

The controversy seems to be between segmental resection and lobectomy, but this is determined by localization of disease segments through preoperative bronchography.

Thoracoplasty as a primary procedure is usually reserved for chronic empyemas or for patients in whom the operative procedure must be done in stages because of decreased pulmonary reserve, resistant organisms, or toxicity. Plombage is useful in poor risk cases and is more widely used than thoracoplasty or in conjunction with thoracoplasty. It is usually used in those patients with low pulmonary function, and in patients with persistent cavitation after a year

of therapy. Cavernostomy is a procedure usually reserved for poor risk patients, ones with large apical or posterior (dorsal) segment cavities.

Cavities of resected specimens will nearly all have positive organisms taken from the cavity wall or surrounding tissue. Therefore, the tuberculous process is inhibited or arrested for a particular time, and the patient is discharged as arrested or cured. At present, the tuberculous lesions are being resected at eight months and those classed at therapy failures at 12 months, these after various trials and readjustments of therapy with newer antituberculous drugs.

Economically, tuberculosis is an expensive disease in hospital costs, wages lost to the patient, and the expense to the community. It seems reasonable that once the disease has stabilized, some form of surgical therapy should be considered, particularly in the younger age group in view of present day knowledge. It is questionable whether or not continuous medical therapy beyond a year has therapeutic value in most instances.

With repeated "breakdown" and prolonged use of antitubercular therapy, chances for a complete recovery are decreased; first, because of developing drug resistance, and second, decreasing patient immunity. Therefore, once a patient has received the maximum benefits of medical therapy, surgical excision of the lesion is indicated. With this policy, the patient can be offered a reasonable cure at an earlier date and returned to society as a useful member.

405 W. 15th St.

### Seminar To Be Held in Las Cruces

The fall seminar of the Dona Ana County Medical Society will be held in Las Cruces Oct. 27 and 28, 1962, with headquarters at the Palms Motel.

Dr. Preston Burnham, Salt Lake City, associate professor of surgery at the University of Utah School of Medicine, will speak on "Injuries and Infections".

A member of the teaching staff of University of Texas Medical Branch at Galveston, still to be selected, will present a paper on burns. There will be no registration fee and physicians attending will receive AAGP credit in Category 1 for seven hours. Sessions will start at 1:30 p.m. on Oct. 27 and at 9:30 a.m. and 1:30 p.m. on the 28th. Information may be obtained from Dr. William D. Sedgwick, 642 S. Alameda, Las Cruces, committee chairman.

A feature of the meeting will be the home-coming game on Oct. 27 between North Texas State University and New Mexico State University.

### Obesity During Pregnancy\*

Treatment With A Sustained-Release
Anorexic Agent

RICHARD X. SANDS, M.D., New York

In a recent study, Reid and his group reported that when pregnancy was associated with obesity the number of complications encountered was appreciably increased and that this increase was also found during labor and delivery. L2 Furthermore, the incidence of perinatal mortality in their cases was substantially higher than among babies born to mothers who were not overweight. This latter observation confirmed similar observations made by others. 3.4 (Table 1)

All the above is rather disturbing to those engaged in any extensive practice in obstetrics, particularly in view of the highly developed state which prenatal care has reached during the past half-century. It is also an indication that obesity during pregnancy should not be treated lightly and should be dealt with more actively than by merely handing the patient a low-calorie diet sheet or by telling her to eat less and then leaving her to her own devices. Unfortunately, this is still all too frequently done.

Another reason for paying extremely careful attention to the obese gravida is the frequent association of overweight and the pre-diabetic state, so-called prediagnosis diabetes.<sup>5</sup> It is not an uncommon experience to become aware of the possible existence of this state, in the obese female, only after the birth of an edematous baby which is either stillborn or dies shortly after birth. In this type of case the fetal mortality may be as high as 28 per cent.<sup>6</sup>

So much importance is attached to weight reduction in the obese diabetic that in diabetotherapeutic circles the maxim, "manage the obesity and you manage the diabetes," has become firmly entrenched.<sup>7,8</sup> Following upon this principle, one investigator reported that the obese mild diabetic makes better progress with weight reduction than with oral hypoglycemic treatment.<sup>9</sup> He employed anorexigenic therapy without diet, a regimen advocated for a considerable time.<sup>10</sup>

In view of the importance attached to obesity control it becomes obvious that treatment should be both rapid and effective, particularly during pregnancy when time-consuming methods appear unsuitable. With this as a guide, a series of experiments was carried out in order to evaluate the rapidity of action and the effectiveness of diethylpropion, an anorexigenic agent, which was administered in the form of a sustained-release tablet\*. The drug was incorporated in a hydrophilic carrier so that release, at a uniformly constant rate, occurred upon exposure to moisture. It was thus hoped to exert a smooth anorexic effect throughout the day. These experiments were part of a long-term study of anorexigenic agents in obstetric obesity control.

#### Material and Method

The entire group treated consisted of 106 cases and included a mixture of racial types selected from the hospital prepartal clinics. Their ages

<sup>\*</sup>From the Woman's Hospital, Division of Obstetrics and Gynecology of St. Luke's Hospital, New York City.

<sup>\*</sup>Diethylpropion for these experiments was supplied in the form of Tenuate Dospan through the courtesy of the Wm. S. Merrell Co. of Cincinnati, Ohio.

Toxemia of Pregnancy
Pre-Eclampsia
Hepatic Disease

Chronic Hypertensive Disease

Increased Fetal Size

Shoulder Dystocia

Higher Incidence of Stillbirth and Meonatal Mortality

Cervical Lacerations

Prolonged Labor

Higher Incidence of Caesarean Sect.

Post-Partum Hemorrhage

Anemia

Higher Incidence of Endometrial Ca

Increased Risk of Surgery

Atherosclerosis

Coronary Artery Dissase

Pulmonary Dysfunction

Gall Bladder Disease

Diabetes

Predisposition to Heat Stroke

Higher Mortality, Hepatic Cirrhosis

Higher Mortality (150% expected rate)

### POSSIBLE COMPLICATIONS of OBESITY DURING PREGNANCY

ranged from 19 to 40 with most of the women being between 25 and 30. The patients varied from gravida 1 to gravida 9, but the greatest number (74) were pregnant for the second, third or fourth time.

A base weight of 180 lb. was defined as obesity for these women and was selected on the basis of height, age and frame structure. This level constituted overweight to the extent of 20 per cent above the average normal weight for the group and for the duration of pregnancy, that is the third trimester. Before treatment the individual weights ranged from 180 lb. to 273 lb. with four patients weighing between 257 and 273 lb.

Diethylpropion, in the form of an easily swallowed 75 mg. sustained-release tablet, was prescribed to be taken daily at approximately 9 a.m. This dose was three times that usually recommended when the ordinary form of the drug is used. Because of the sustained-release principle, it was expected that there would be sufficiently high drug levels to control appetite throughout the remainder of the day. However, when it was felt that a sufficiently strong anorexic effect was not being exerted, the dose was increased to 2 Tabs. and even 3 Tabs., daily.

No form of dietary restriction was employed. Patients in the study were kept unaware of the fact that an anorexigenic agent was being used and that obesity control was being attempted. They accepted the new tablet as another aspect of their prenatal care. This served as a form of control and lessened the likelihood of a placebo effect. A further form of control was introduced when medication was stopped, for some reason, and weights were found to increase beyond the amount expected, normally.

Treatment was maintained for intervals of three to 17 weeks. (Fig. 1) Any patient who did not have at least three weeks of medication was not considered to have had an adequate test of therapy and was, therefore, not included in the final evaluation.

These patients were treated entirely during the third trimester, the period of greatest weight increment, and the results were evaluated by means of an original method, fully described elsewhere. <sup>10</sup> In short, the normal average weekly increment (0.86 lb.) is multiplied by the number of weeks of therapy and this is added to the weight at the beginning of treatment giving a figure termed the expected weight. This figure is then subtracted from the actual weight, at the end of treatment, and called the weight benefit. If the weight benefit is negative the result is considered successful, if positive it is a failure. All the individual weight benefits are then statistically analyzed.

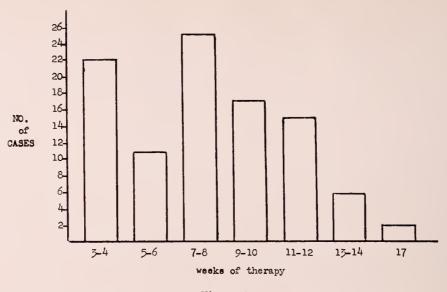


Figure 1

As stated above, 106 patients were originally included in the experiment. Of these, eight delivered before having had at least three weeks of treatment and are, therefore, not included in the final evaluation. In the remaining 98 cases, treatment was continued until the onset of labor.

#### Results

Of the 98 cases left for final evaluation 86 were successful, that is to say they showed a negative weight benefit at the time labor set in. The success rate was 87.7 per cent. Of the failures, four women admitted to not taking the medication as prescribed and two others only reached their expected weight so that their weight benefit was 0. These are included with the failures for the sake of completeness. Another patient in this group complained of nausea and insomnia and it was suspected that she did not take her tablets regularly. Statistic analysis of the results showed them to be significant. A comparison of the expected and actual weights is of interest, showing a distinct downward trend in the entire group. (Fig. 2)

The incidence of side-effects was singularly low, for an agent of this sort, and the incidence corroborated similar results reported by others. These pregnant women did not appear to be greatly disturbed by them. Of those reported, insomnia was the most frequent. Nausea, dizziness and diarrhea were each reported by one patient, respectively. Another patient complained

of palpitation which disappeared when she stopped taking coffee. In contrast to the above, another woman volunteered the fact that the new tablets made her "feel so good".

There were 32 babies who weighed over eight pounds, in the entire series, an incidence of just over 30 per cent. Of these, four weighed over nine pounds, two over ten pounds, and one weighed 11 pounds, four ounces. There was no indication of overt diabetes in any of these mothers. However, during pregnancy, two of them had a high level of glycosuria which, on further investigation, turned out to be of no diabetic significance. One was the mother of the 11 pound baby. In addition, the grandfather of one of the nine pound infants was a diabetic.

Four patients in this series had been successfully treated with anorectic agents for obesity, during a previous pregnancy. On this occasion, one of them was diagnosed as a mild diabetic and although responding to the present treatment she was, nevertheless, placed on a 1500 calorie diet, at 33 weeks, and delivered of a 5 pound, 10 ounce baby, at 38 weeks, by Caesarean section, for cephalopelvic disproportion.

One of the women, not included in the final group because of insufficient therapy, developed episodes of bleeding during the 29th week of pregnancy. A diagnosis of marginal placenta previa was made and after admission for observation she delivered herself, spontaneously, of a 3 pound, 2 ounce baby which survived.

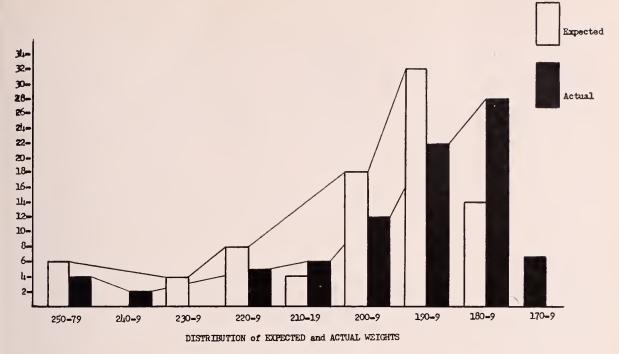


Figure 2

Ten cases developed mild pre-eclampsia, an incidence of just over 10 per cent, which is higher than that observed in the pregnant population, as a whole.<sup>12</sup>

Experience with dosage was instructive. All patients started diethylpropiontherapy with an initial dose of 75 mg. However, only 50 cases completed treatment at this level. In the other cases, because it was felt that a sufficient anorexic effect was not being obtained, the dose was increased to 2 Tabs. in 42 cases and to 3 Tabs., daily, in 14 cases. In only two instances was it necessary to reduce the dose, because of insomnia in one and because the other complained of a "druggy" feeling.

### Discussion

Individual patient dosage is an important aspect of drug therapy which holds equally well for anorexigenics. It is a universally recognized pharmacological principle that size and body weight influence dosage<sup>13,14</sup> and it is, therefore, not surprising that many of these markedly obese pregnant women should require larger doses than a moderately overweight non-pregnant female.

It has been our clinical experience that the type of patient treated in these experiments is able to tolerate large doses of appetite-depressant drugs without trouble and without apparent harm to the fetus.<sup>10</sup> This was borne out in the present series in which more than half of the entire group did well on two or three times the recommended dose. Furthermore, side-effects did not appear to be related to dosage since there were as many instances with a small dose as there were with larger ones.

Although it is generally thought best to obtain obesity control and weight reduction by dietary means, it is naive to look upon this as a simple, rapid and effective method during pregnancy. Very little experience is necessary to realize how disheartening and disappointing this form of treatment can be for both patient and doctor. A great deal of time and patience are necessary in order to obtain even minimal results by merely limiting the amount of a patient's normal diet.

In many of these cases, other people had unsuccessfully attempted to obtain obesity control by means of diet alone. Even successful drug therapy resulted in recurrence. Although only four such cases are reported here, many have been encountered in other sets of experiments. Such experience almost forces one to the conclusion that obesity may be an incurable form of malnutrition similar to tobacco habituation and alcoholism. After all, no amount of drug therapy will alter the patient's personality pattern or her general environment.

On the basis of continued and increasingly extensive clinical experimentation in treating obstetric obesity it appears that better and more rapid control is obtained with so-called 'tough' methods. These seem to be more acceptable to the patient.<sup>15</sup> Furthermore, no additional tension is introduced by interference with the patient's normal domestic background if non-dietary methods are used. Her environment is already sufficiently disturbed by the pregnancy and by the imminent addition of another member to the family group.

Although the response to diethylpropion therapy was good, as evidenced by the high success rate, the 30 per cent incidence of large babies was, nevertheless, surprisingly high and greater than that previously reported. This incidence appears even higher when considered in terms of Reid's recent report that the reduction of maternal obesity seems to bring the mean fetal weight into normal ranges.

In the present series, weights had been increasing steadily until the exhibition of diethylpropion. Since neither dietary restriction nor the anorexic nature of the new tablet had ever been mentioned, it is reasonable to attribute any control of obesity or actual loss of weight to drug action. The fact that weight again increased, pari passu with cessation of drug therapy would tend to strengthen the above assumption. This is, essentially, the technique of animal experiment. This type of control was exercised in 21 cases. Medication was stopped for intervals varying from two to 21 days. In every instance there was a weight increase which ranged from one to six pounds.

### Summary

- 1. A series of 106 obese pregnant women were treated with diethylpropion, an anorexigenic agent, in a new sustained-release form.
  - 2. No dietary restriction was imposed.
  - 3. The success rate was 87.7 per cent.
- 4. There was a strikingly low incidence of side-effects.
- 5. The effect of this type of therapy, upon maternal and fetal weight, is discussed.

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### Dr. Papper Named To U. of N. M. School Of Medicine

Dr. Solomon Papper, former Professor of Medicine and Professor and Chairman of the Department of Preventive and Environmental Medicine at the Medical College of Virginia in Richmond, has been appointed Professor and Chairman of the Department of Medicine at the University of New Mexico School of Medicine in

Albuquerque, according to an announcement by Dr. Reginald H. Fitz, Dean.

Dr. Papper assumed his duties on Sept. 1. He is principal investigator under a grant from the National Institutes of Health to support a study on the Kidney in Cirrhosis and Sodium Excretion in Hypertension. This study will continue at the University of New Mexico.

### Emotional Disorders in the Family Physician's Office\*

(Final Section)\*\*

WILLIAM F. SHEELEY, M.D., F.A.P.A., Chief, American Psychiatric Association General Practitioner Education Project, Washington, D. C.

In his enthusiasm to find patients with emotional disturbances in need of attention, however, the physician should exercise some restraint. As Counihan<sup>10</sup> warns:

"It cannot be too strongly emphasized that few patients will be found lacking in a neurotic basis for symptoms if one is sought. It requires great skill to decide who has a sufficiently stable personality to make neurotic symptoms unlikely. I believe the pendulum has swung too far and the mistake of treating organic disease by psychotherapy is now as common an error as the much derided mistake of treating psychogenic symptoms as physical disease."

An example of this hard-headed and practical attitude is provided by Asher<sup>2</sup>:

"One young woman referred to me . . . was a bit of a problem child; she had been more or less bald for several years and (her doctor) suspected the condition was due to trichotilomania (dermatologese for hair-pulling) . . . at our first interview I asked her if it was possible she was occasionally pulling hairs out of her scalp. She said yes, she thought she was, I then said that as it seemed to be making her bald it might be a good idea to stop pulling her hair out. She said, all right, she would try. That was the only treatment given . . . she had a normal head of hair within three months."

Having found a case of psychiatric illness among his patients, where should the physician have it treated? This, of course, will have to be determined for each individual patient. Treatment in the community, however, is usually not only feasible, but most desirable. Speaking of the home care of psychiatric patients in Great Britain, Little<sup>37</sup> says:

"No review of this subject can do other than make early reference to the experiments in community care of the mentally sick carried out in recent years at Worthing . . . in a nutshell, it was there demonstrated that by providing adequate alternative care through intensive home visiting, out-patient services and day-hospital facilities it was possible to reduce the annual admissions to mental hospital from a large geographical area to 40 per cent of what it was previously and further, that this approach was preferred by patients and relatives alike.

"There is now widespread professional acceptance of the theme that much wider home care and treatment is practical and desirable. It demands tolerant concern from all parties — relatives, friends, employers and professional people. Treatment in the home in the light of the newer treatments and attitudes to mental sickness is a stimulating medical and social challenge in which the family doctor must play a key role. In so doing, he may find increasing satisfaction in a sizeable section of his life's work which has previously in varying degrees been a source of irritation, frustration and embarrassment."

Another important psychiatric function of the family physician is preventing mental illness among his patients. We have already suggested that early detection of incipient trouble in an individual may prevent invalidism. The physician can also discover incipient trouble in the family and in the community.

Certainly, as Warkentin<sup>53</sup> says, the family has crucial importance to the emotional health of its members:

"There is a growing conviction that many patients are so closely intertwined with their fam-

<sup>\*</sup>Presented at the first annual New Mexico Psychiatric Seminar, Las Vegas, N. M., March 11, 1962.

<sup>\*\*</sup>Section one published in Sept., 1962, issue of Southwestern Medicine.

ilies and other associates that it is not possible to treat them without including 'psychological relatives' in the treatment effort."

Let us look at a few examples of how the family affects the person:

Brown<sup>6</sup> discovered that as children, a large percentage of depressed patients had lost one or both parents. Loss of the mother is serious at any age. Loss of the father before the child is five years old is apparently less important than is such loss during the ages five to 14. When such loss occurs Brown urges that an adequate parent substitute be obtained promptly.

If one or both parents is psychotic, the children are affected. In a controlled study of 330 children of psychotic parents compared with 342 children of normal parents, Cowie<sup>12</sup> found no evidence 'on a genetical basis of a raised incidence of neurosis . . .' She did find, however, 'evidence supporting the environmental hypothesis that psychosis in a parent is conducive to neurotic disturbance in a child.' When one of his patients developes a psychosis, then, the physician will concern himself with the effect of that psychosis on the patient's children."

School phobias, according to Levenson<sup>36</sup> may reflect a home situation in which a dominant and scornful mother has overwhelmed a passive father.

#### Demands

Parents may make a schizophrenic youth worse by making impossible demands on him. Haley<sup>23</sup> says:

"If the child seeks closeness he is encouraged to be at a distance. If he attempts to put some distance between himself and his parents, they respond as if they have been criticized and indicate he should seek closeness. If he asks for something, he is too demanding—if he does not ask, he is too independent . . . what other parents would consider normal behavior, such as the child making demands upon them, criticizing them, objecting to what they do, asserting his independence, and so on, these parents consider impossible behavior."

Relatives may even, according to Fellner<sup>19</sup> provoke suicide attempts in a family member.

A most suitable doctor to deal with these family

influences on a patient's illness is the family physician who is alert to the dangers, and who has developed the skills to cope with them. As Parloff<sup>48</sup> says:

"Today, more and more practitioners are attempting to deal with the family as a unit.

". . . the diagnosis of pathology must involve the assessment of the internal organization of the family, parental roles, child-rearing practices and how they are integrated at each step of the child's development.

"The main stream of theory has moved from the position that the solution lay in the comprehension of the individual's intrapsychic conflicts, to the hope that an understanding of the interpersonal relationships between the patient, a parent, and others would improve the effectiveness of therapy."

The physician should deal with the family not only in cases of psychiatric illness but in all illness. As Laughlin et al<sup>33</sup> remind us:

"No sick person is influenced solely by his physician. Every patient is also influenced by his family. They often become overly anxious and unintentionally intensify his illness. If he does not improve . . . quickly . . . they may question our competence, our interest, or our understanding of his sickness. They call upon us for information, for advice and for reassurance. They may interfere . . . seriously with our treatment . . . the amount of our professional time consumed in behalf of the relatives may far exceed that which is needed for the patient."

#### Environment

As the physician works with the family he must also be cognizant of the influence and effects of the larger environment; he must also work with the community. Hinkle<sup>24</sup> therefore says:

"The physician who is charged with the preservation of health and the treatment of disease, will concern himself with man's relation to his social environment when this is relevant to his health. If he intervenes in this relation, we can expect that he will do so as a physician acting to preserve health or to treat disease. This may make it necessary for him to acquire special skills, but it will not require him to create a new kind of medicine."

And Farnsworth<sup>18</sup> adds:

"... the promotion of mental health—and to a large extent the prevention of mental illness is a responsibility shared by all physicians ... physicians regardless of their special professional interests and practice, should be particularly effective leaders in mental health promotion in their own communities."

#### Aging

The family physician may, for example, help the community more healthfully handle its aging members, as Schultz<sup>52</sup> points out, if the aging person recognizes that his role in society is changing, and if he finds and accepts one of many opportunities a wholesome community will offer him to play a useful and respected role, he will find growing old less of a burden to himself, to his family, and to his community.

In many ways, as Davies<sup>13</sup> suggests, old age is itself a psychosomatic condition which is critically influenced by the way the community treats the old person:

"At present, one of the hazards of old age is that loss of (physical) health may not come alone, but may be accompanied by loss of occupation, income, status, friends and sometimes spouse . . . the crippling effect of all these stresses on mind and body leads not infrequently to old age itself having to be regarded as psychosomatic."

The physician, in his efforts to prevent psychiatric disturbances from developing among his patients, must also look to himself. While treating an eye condition, for example, the unwary physician may plant the seeds of neurosis, according to Kaplan and Milder<sup>26</sup>:

"If the doctor dismisses the patient's problems as 'just nerves,' he is endeavoring to make his own escape from the realities of the situation with which he is confronted. On the other hand, it is often tempting to skirt this relatively uncharted area by resorting to the clear-cut, precise solutions of spheres and cylinders. In either event, the patient receives neither sympathy nor truth . . . the unnecessary prescribing of glasses for such patients is an open invitation to the dissatisfied patient to avoid confronting his problem."

The heart may become the focus of iatrogenic neurosis. As Knight<sup>29</sup> warns:

"To tell a patient he has a 'nervous heart' is . . . poor judgement, because this places the emphasis on the somatic rather than the psychological aspect of the illness. One should try to help the patient understand that it is his personality which is sick, not his heart."

Or the physician may, points out Brookes<sup>5</sup> find himself in a bewildering and frustrating game of cat-and-mouse with his patient:

"A phobic individual is extremely sensitive to every sign that reinforces or abates his fear. Thus he responds to the words 'its only nerves,' but not for long. He is soon back for another dose of reassurance. And he accepts 'there's nothing wrong,' but his reservations to this denial of his symptoms grow just as soon as he fills a prescription for an expensive tranquilizer. When he again reports to the doctor and receives a different tranquilizer, his fears will not be quieted. When he phones to report on how badly he feels and the physician accommodatingly suggests he come to the office, then he feels things are bad indeed."

#### **Excellent Position**

I have suggested that the family physician is often in an excellent position to prevent and to treat the psychiatric illnesses and emotional disorders of his patients. He occupies this position partly because psychic and somatic illness so often co-exist, and are therefore logically treated simultaneously by the same physician. Sometimes, shall we say, specialization loses more than it gains, Knutson<sup>30</sup> says:

"Many of the ills of modern society stem from attempts to deal with man segmentally rather than with man as a unit. Specialization, which seems to be the inevitable outgrowth of scientific advance, results in institutions competing with one another for primary segments of an otherwise unified man. How far removed are we from the medicine man, who for all his weaknesses, sought to treat the total man! He had strengths which have not been duplicated in our modern society."

Furthermore, the family physician has what is needed for this comprehensive therapy. As Masserman<sup>40</sup> tells us:

". . . the science and are of clinical therapy consist of the following essentials: First, the maintenance of the scientific prestige, ethical integrity and social influence of the psychiatric and allied professions and the individual therapist . . . Second, the warm, unashamedly personal acceptance of each patient, not as another 'interesting case' . . . or as an object of 'objective diagnosis,' or even as grist for another therapeutic mill, but as a hurt, frightened and troubled human being seeking relief and guidance."

The family physician can bring to his treatment a humanistic quality, which Allen<sup>1</sup> defines as:

". . . a quality of the physician who translates to the patient, in the process of giving evidence of his skill, that he regards the person, the human being, as the important factor in treating disease."

#### Uncertainties

I would, of course, be fatuous to suggest that providing such comprehensive care is not without its questions, doubts, and uncertainties. Some of those problems are posed by Gee<sup>20</sup>:

"The fault lies not in a confusion of ultimate aims, but in a confusion of knowledge and beliefs with respect to what comprehensive care is, what can or cannot be taught, and who should teach. Which aspects of these problems are rooted in philosophy and which in science? To what degree is patient care a function of the physician's medical knowledge, of his attitudes, and of his basic personality structure? To what degree should it also be a function of a scientific knowledge of the psychology of human behavior and of knowledge of sociology or of the development of skill in communication and in manipulating patients' emotions and attitudes?

"Humanitarian concern with the welfare of the patient has been thoroughly confused with knowledge of psychological and sociological components of organic disease processes, and both of these have been confused with how skill in dealing with the personal and emotional problems of patients may be developed."

Nevertheless, the family physician has a 'public image' that gives him a distinct advantage over many other people for providing medical care that embraces both the somatic and the psychic. As Merloo<sup>41</sup> describes this special status of the physician:

"In his battle for greater security man selected for himself some wiser, more experienced fellow man—a magician or shaman—who could show him the narrow road to follow through life. However, in man's battle for a secure dependable relationship to his fellow man, the other fellow's greater knowledge, greater insight, and greater persuasive power could in themselves become a new danger . . . he (the doctor) was the helper, adviser and giver of solace; yet he inspired awe and anxiety. Somehow, behind medicine always hovered the fear of death . . .

"We are not yet out of the epoch of magic thinking . . . when no antibiotic is given for the common cold, the doctor is criticized and condemned—though the stuff does not work. The physician himself inadvertently indulges in the magic of prescription: no man with evil or depressed mood can pass him with the prescription of a miracle drug."

Watts<sup>54</sup> cautions us not to lose sight of this special magical quality of the physician as we move more deeply into the use of drugs and similar therapeutic approaches. He says:

"Besides the drug, the patient needs the personality of the doctor behind it. One source of comfort does not exclude the other—they must be added together and used together."

On the other hand, the physician should not hesitate to use drugs when they will ease the patient, or otherwise facilitate therapy. Phillips and Shoemaker<sup>50</sup> remark that when the patient is unduly alarmed by organic disease and cannot be readily soothed by supportive measures such as encouragement and sympathy, a sedative or an ataractic drug may be very helpful.

Such use of drugs to supplement other psychiatric therapies is becoming ever more widespread among psychiatrists. Morrow<sup>42</sup> reports that:

"... some patients even in psychoanalysis are now being given selected drugs with benefit. Many of us feel that pure psychotherapy (as was formerly practiced almost exclusively) is not entirely the sine qua non of rational therapy."

Fortunately, a large number of good psychiatric drugs are presently on the market, and new ones are appearing almost daily. Very often, the psychiatric patient's condition may be such that he cannot economically be given traditional psychotherapy by the psychiatrist. In fact, good sense

may well dictate that he not be treated at all by a psychiatrist, but by his family physician. For example, Nodine<sup>45</sup> reports:

"The Psychopharmacology Research Program at Hahnemann Medical College is currently being carried out with a group of chronic psychoneurotic patients who may also have medical problems. These patients have been evaluated by a psychiatrist and are not found to be suitable for psychotherapy. As a result, our use of various psychopharmacologic agents in a large group of such patients with varying types of psychologic problems, including anxiety, tension, conversion reactions, situational reactions, depression and character disorders fills a kind of 'no-man's-land' in the patient therapy; these are the difficult patients who visit the average physician's office."

These drugs are not only becoming more numerous, they are becoming more specific. They therefore are becoming ever more useful to the family physician. In this connection, Cooper<sup>9</sup> says:

"The central nervous depressants, like chloral and amylene hydrates, paraldehyde, bromides and even barbiturates . . . are giving way . . . to therapeutic agents whose target areas in the central nervous system grow ever more and more narrowly defined, until it has become practicable to depress or excite one area of the brain tissue without unwanted effects upon adjacent areas."

Polonio<sup>51</sup> gives us an example of this specificity:

"Hydrazine derivatives, for instance, function as activators and disinhibitors, increasing the energy output. Imipramine . . . seems to produce a damping down of emotional reactions, possibly resulting in emotional flatness. We use hydrazine derivatives in asthenic, insecure, obsessive and phobic personalities as well as in fatigue and exhaustion states . . . we use imipramine in patients with depressive, obsessive, anxious features, particularly when sthenic characteristics are seen."

Time will not permit us to go further into the details of drug therapy, and the wide variety of psychiatric preparations available. Permit me, instead, to refer you to the review by Detre and Jarecki<sup>15</sup> in the September, 1961, issue of *Connecticut Medicine*.

Now, that aspect of psychiatric treatment which may cause the family physician the greatest feeling of insecurity is psychotherapy. Perhaps he will want to keep one foot planted firmly in somatic therapies while tentatively resting his other foot in psychotherapy. This, really, is a good approach. As Kraft and Blumenthal<sup>32</sup> suggest:

"The patient's emotional relationship to the doctor can have a psychotherapeutic function. If the doctor continues to emphasize during visit after visit that he understands how emotional tension is keeping the patient upset and his allergies active, and if he points out that the immunologic and pharmacologic therapies also have their value, then the patient benefits emotionally from the relationship. Physicians who have had training in psychotherapy may go even further than this. While they continue their immunologic and pharmacologic therapies, they also discuss emotional problems with the patient."

Or the physician may want to deal with such problems as frigidity in his patients. This also can have great value for the patient. As Kleegman<sup>27</sup> says:

"It is the general practitioner who sees most of these problems and who could do the greatest good if he were educated in this phase of medical practice. Only a small number of women have frigidity as a part of neurosis so severe that they need referral for the necessary psychiatric treatment. The general practitioner could be taught to differentiate one from the other."

In any case, Gledhill<sup>22</sup> encourages the physician to have modest goals for his psychotherapy of the patient. Many psychiatric conditions, after all, are chronic processes that defy the therapeutic strategies of the most astute psychiatrists. Often we have no choice but to accept certain psychiatric limitations in a patient—see them as immutable—and try to help the patient and his family accept those limitations. This is really the kindest and most helpful contribution that we can make.

Having examined these background considerations of psychotherapy by the family physician, perhaps we might examine a little more closely just what kinds of psychotherapy the physician might offer.

Little<sup>37</sup> admonishes the physician to realize that the psychotherapeutic process starts with the very first contact of patient and doctor—unless it in fact, actually starts before. He says:

"The initial interview with the patient is of su-

preme importance. It greatly helps the patient's morale if he can be given time to unburden all his major anxieties at one sitting and to feel that the eloctor is in possession of all the relevant facts. It is at this interview that the eloctor sifts all these facts and makes his diagnostic formulation . . . it has been claimed . . . that to set aside an hour for such patients yields superior therapeutic results and saves time in the long run, for such an interview builds confidence to a point where the repeated, fruitless, mutually frustrating, importunate demands for help are diminished.

Maholick and Warkentin<sup>38</sup> suggest that the interviews be brief, and that the psysician charge a fee for psychotherapy just as he does for any other use of his time. They say:

"Very brief interviews which are properly structured in keeping with known psychiatric principles, and for which a reasonable fee can be charged, can be a most valuable adjunct in any doctor's office.

"1. Always charge a patient for psychiatric interview, otherwise doc will feel like an amateur and resent it, too. 2. In dealing with emotional disorders, the basic therapeutic tool is the interview. 3. Some doctors set aside two hours on same day each week specifically for psychiatric interviews. 4. Schedule 10-15 minutes per patient. 5. Protect the interview from interruptions. 6. Don't talk to patients at home or outside of office hours. 7. Do physical exam, etc., at another time. 8. Listen more than talk."

In his psychotherapy, especially with such patients as those with chronic schizophrenia, the physician can use his traditional attitudes and techniques. As Brody<sup>4</sup> says (paraphrased):

"The doctor acts like a busy practitioner—sees patient for short visits (15-20 minutes) that do not encourage too much closeness in relationship. Presents himself as a real person. Doesn't hesitate to use medications which support patient even though they may be placebos in effect. Doesn't hesitate to hospitalize patient (preferably in general hospital instead of mental hospital) when acute flare-ups occur."

Mandell<sup>39</sup> supports Maholick and Brody in recommending the 15-minute interview. He believes that such an investment of the physician's time yields the greatest return per hour expended. During such brief interview he suggests that the doctor (paraphrased):

"1. Emphasize the patient's strengths. 2. Reinforce his defenses against anxieties. 3. Help him learn to live with unchangeable neurotic symptoms. 4. Maintain warm but formal relationship."

And Allen¹ emphasizes the value of these psychiatric principles to the doctor dealing with children. Assuming that many of the children's life stresses go back to anxieties in the parents, Allen suggests that the doctor deal with these parental anxieties by listening to the parents and by reacting to them in a natural way. He urges the physician to reassure the mother who is trying too hard to be a good mother.

He should tell her that the child may well profit if she simply relaxes and enjoys him. Allen even suggests that in the long run hospital routines may be less disrupted if, when a child must be admitted as an in-patient, his mother be permitted to accompany him to the pediatric ward and to help the nurse get him bedded down in his new and terrifying surroundings.

Increasing attention is being paid, of late, to the doctor-patient relationship. Such attention is most proper because this ubiquitous, frangible, and yet powerful thing often determines therapeutic success or failure. Now, this relationship is basic to all psychiatric therapy, to be sure, and it is just as basic to the other medical therapies.

The most skilled surgeon may see his handiwork fall apart on the rocks of a bad doctor-patient relationship; the internist may find that regulating this relationship will as quickly stabilize a diabetic patient as well as regulating insulin and diet.

As Gerty<sup>21</sup> puts it, all medical therapy contains psychotherapy, and that is dependent on the doctor-patient relationship. In order to discover the information that he must have in order to treat even somatic disease adequately, for example, the doctor must encourage his patient to tell him things that the patient had rather conceal. Such candor requires a trusting doctor-patient relationship.

This relationship, alas, is not always what we should like it to be. Perhaps at times the fault lies mostly with the patient. As Whitehorn<sup>55</sup> observes:

"The doctor expects docility in a patient, but this expectation is not always fulfilled, even in the state of accentuated dependency imposed by illness. The 'uncooperative patient' is perhaps the commonest problem about which the doctor feels consciously and distressingly challenged regarding his knowledge of human nature and his skill in human management.

"No less troublesome . . . is the tremblingly cooperative patient, frightened into extreme docility, full of apprehension, whose slightest ache . . . is magnified by . . . his dread of the potential implications. By such a patient, the doctor's every word or gesture is anxiously scrutinized for intimations of cancer; the doctor's kindest ministrations are loaded with foreboding and threat, and every test procedure arouses fresh apprehensions of disaster.

Or, as Knight and Baird<sup>29</sup> remind us, the relationship may be distorted by dependency problems of the patient:

"Among those who crave dependency are (1) those who were overprotected as children and conditioned not to want to leave a protected environment; (2) those whose dependency needs were never quite satisfied . . . in childhood . . .

"Among those who are afraid of dependency are two principal types: (1) Those who avoid help because they are afraid of dependency . . . they fear injury or sickness because it will make them helpless, like infants who can be abandoned or rejected by the strong around them . . . it is not that they dislike dependency, for they do, but they are frightened by what may happen to them in the dependent state. (2) Those who avoid help because they are ashamed of helplessness. In childhood such persons . . . were pushed prematurely into independent activity. Thus they learned early to be ashamed of their helplessness . . . long before they fully recover from an illness or injury they are back at work."

On the other hand, the doctor may himself upset the relationship. For example, in giving psychiatric therapy, the physician somehow trades his easy, old familiar role for one that seems to fit most uncomfortably. Gledhill<sup>22</sup> has this to say:

"One of the difficulties about the practice of psychotherapy is that in only some forms of psychotherapy can the doctor maintain his traditional role. In this role, the doctor is regarded by his patients as an all-powerful benevolent person whose word commands great respect, and this is a position which a doctor naturally strives to keep and he almost comes to believe in it himself. When he meets an illness which he cannot fully understand, especially psychological illness, this role begins to be threatened."

Davis<sup>14</sup> describes in some detail how the doctor feeling uncomfortable may contribute to deterioration of the doctor-patient relationship. He says the doctor may be:

"Drawn into making remarks which, on reflection, he might have preferred not to have uttered, or because of this emotional involvement he misses significant features of the patient's talk. This is especially likely to happen (a) when the doctor is a man and the patient a pretty girl, (b) when the patient has a dramatic problem, often of a sexual nature. (c) with a dying patient when the doctor's own guilt feelings are involved. (d) in the case of the self-deprecatory patient who bolsters the doctor's self-esteem, or (e) when the patient has special knowledge of a subject which coincides with the doctor's own personal interests."

Davis also gives us some danger signals of trouble with the doctor-patient relationship:

"Lengthy interviews, giving up vacations, making arbitrary decisions outside one's province, oversympathizing with patients, making frequent changes in treatment, being angry with patients, feeling unduly guilty about patients, giving or accepting expensive gifts may all be indications of an unhealthy atmosphere existing between a doctor and his patients...

When he has relationship problems with a patient, the physician may profitably talk the matter over with another physician in whom he has confidence, or with a psychiatrist if one be available to him.

Not too infrequently, failure to make progress in psychiatric therapy stems not from difficulties with the relationship but from the simple inability of presently available therapies to cure all psychiatric disorders. The doctor may then have to recognize that disposition of the patient is the most constructive next step in his management. As Cowen<sup>11</sup> puts it:

"Non-psychiatric colleagues must understand, however, that having reached an appreciation of the patient's psychodynamics does not mean necessarily that 'cure' is possible by psychotherapy. Sometimes the problem becomes one of disposition, with social service having to play the intermediary role; sometimes supportive out-patient or family physician care is all that the patient can accept; and sometimes . . . a 16th surgical operation can be averted."

I suppose so much has been said about the many evils of referral—of dumping difficult patients on other doctors—that the doctor is often reluctant to refer a patient to a psychiatrist. When a referral serves a constructive therapeutic end, however, and is astutely carried out, the doctor need have no qualms. Referral can be a very useful step in the management process. The important thing is that the physician make the referral to help the patient—not to reject him—and that he have a productive working arrangement with the psychiatrist to whom he refers the patient.

The attitude of the doctor at time of referral deserves underscoring. As Farnsworth<sup>18</sup> says:

"If by their manner they convey irritation and a negative attitude . . . the psychiatrists who then see the patients have to devote much energy to gaining their confidence and calming their fears. On the other hand, if referring physicians look upon psychiatry as a medical specialty like any other . . . patients who are referred will be given the impression . . . that the experience will be of value . . . "

Furthermore, the presence of mutual understanding and assistance between psychiatrist and referring physician are essential. This understanding does not always prevail. Coleman and Errera<sup>8</sup> found (paraphrased):

"1. Physicians know little about psychiatry, fear the patients, and think psychiatry has nothing to do with medical practice, 2. Psychiatrists tend to take over the care of the patient and to exclude the physician (although he is often glad that they do). This isolates the psychiatrist, 3. The phychiatrist is effective only if he learns the skills of working with other physicians."

In this connection, the community general hospital with a psychiatry service is proving to be an effective meeting place between psychiatrist and

other physicians. Working together as they most naturally do with patients having simultaneously both somatic and emotional problems, the psychiatrist and his medical colleague come to know one another personally and to develop channels of medical communication which serve the referral process.

#### As Eaton<sup>16</sup> says:

"Since nearly all (psychiatric) patients are first seen by their family doctors, changes in treatment facilities are important to the practitioner. The open ward should make it easier for patients and their families to accept a recommendation for hospitalization..."

After such working relationships have been established, the office therapy of emotional disturbances by the family physician acquires a new dimension of scope and excellence. When a patient's acute psychiatric exacerbations require specialist attention or even brief hospitalization, the physician calls in his psychiatrist colleague. The two physicians then work together; each applies those skills which are his particular forte. The psychiatrist, for example, may give the patient electroshock therapy while the family physician both gives the patient personal support and helps the family through the crisis. As the patient recovers from the acute exacerbation, the family physician resumes primary responsibility. Having kept fully informed about the patient before, during, and following the acute episode, and being able to confer regularly with the psychiatrist, the family doctor is in the best position to do what is needed, at the right time, and in the proper amount.

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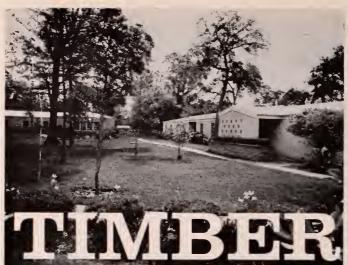
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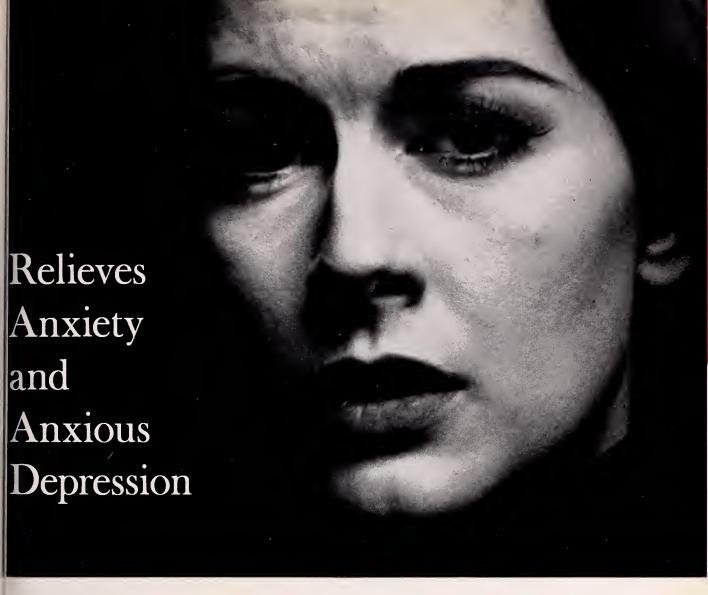
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- 1. Demeulenaere, L.: Action du R 1132 sur le tronsit gostrointestinol, Acto Gostroent, Belg. 21-674-680 (Sept.-Oct.) 1958.
- Kosich, A. M.: Treolment of Diorrheo in Irritoble Colon, Including Preliminary Observations with a New Antidiorrheal Agent, Diphenoxylate Hydrochloride [Lomatil], Amer. J. Gostraent. 35:46-49 (Jan.) 1961.
- 3. Weingarten, 8.: Weiss, J., and Simon, M.: A Clinical Evaluation of a New Anti-diarrheal Agent, Amer. J. Gostraent, 35:628-633 (June) 1961.

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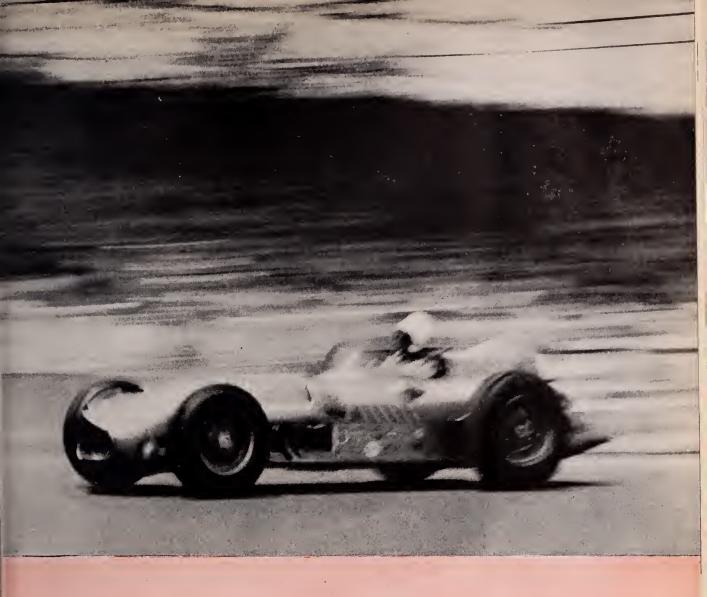
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1. Dupler, D.A., Greenwood, R.J., and Connell, J.T.: J.A.M.A. 174:123 (Sept. 10) 1960.

2. Hobbs, L.F.: To be published.

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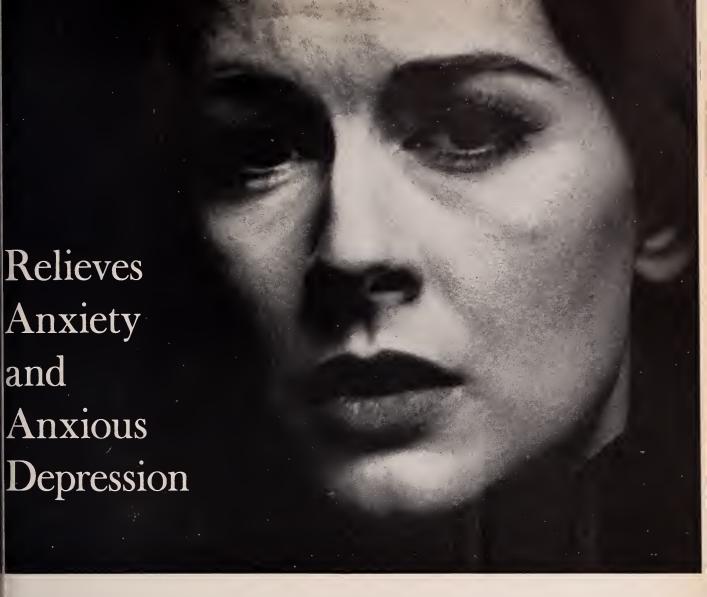
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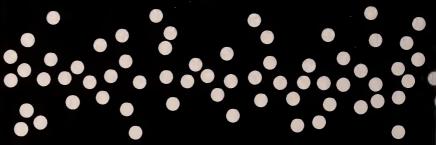


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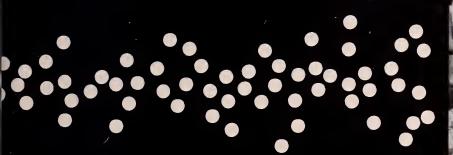
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1. Hodges, F. T.: *GP* 14:86, Nov., 1956, 2. Guild, B. T.: *Arch. Dermat.* 51:391, June, 1945.

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#### Bothersome Bleeding

May 22, 1962 St. Vincent Hospital Santa Fe

Case Presentations: Richard M. Angle, M. D.

Discussion: Armand J. Quick, M. D.

Marquette University School of Medicine, Milwaukee

Dr. Angle

Case  $\pm 1$ : D.S.

This 18 year old white female patient entered the hospital on 10.10.60, with a history of two fainting episodes, the first of which occurred in February of 1960, and the second of which occurred on the day of admission. Her only other complaints were of pallor and fatigue.

Her past history revealed only the usual child-hood diseases and bronchial asthma at age 3-4. The patient stated that for several days prior to admission she had noted a fine hemorrhagic rash over the skin of the lower legs. Her family history was normal.

Physical examination revealed normal vital signs; there was moderate pallor. There was no adenopathy or splenomegaly. A fine purpuric rash was noted on the lower legs with a few purpuric lesions on the arms.

Laboratory studies on admission revealed a hemoglobin of 8.2 grams, packed cell volume 26 per cent, WBC 6,050. RBC 2.81 million. Coagulation time, 15 minutes, bleeding time, five minutes and 30 seconds. Differential blood count was normal; no platelets were seen. Clot retraction was 0 in 24 hours. Urinalysis was normal. A stool was positive for occult blood and L. E. Cell test was negative. On 10.12.60 the platelet count was 2,600 per cu. mm. and on 10.13.60. 6,000 per cu. mm.

The patient was placed on prednisolone 100 mg. daily with a rise in platelets and was discharged on maintenance prednisolone.

On 11.16.60, she was readmitted because it had been found that large doses of prednisolone were necessary to maintain normal platelet count. On 20 mg. per day, her platelet count was 75,000, while on 15 mg. per day it dropped to 18.000 and was associated with bleeding from the gums. A bone marrow study was normal except for megakaryocytic hyperplasia and her platelet count on admission was 75,800. A splenectomy was performed without incident and was followed by the expected rise in platelet count to over 1,000,000.

Postoperative course had been normal and there has been no recurrence.

#### Dr. Quick

If we had done a prothrombin consumption time we would have found that it would have been very low. There is one other test we always like to do and that is the tourniquet test. It is quite informative. The correlation between the platelet count, the tourniquet test and the bleeding time very often agree, but many times they do not and I don't know the reason why.

The coagulation time of 15 minutes worries me. We should have a dictator to make all of us use a uniform test when we do clotting times. This test of 15 minutes doesn't give us much information. In some laboratories it may be normal, but in some laboratories it may be abnormal. Temperature is a very important factor in the clotting

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time and if you have "room temperature", that again depends on whether you're in my laboratory during winter time or summer time. There's quite a variation. The clotting time should be done at a fixed temperature and I like 37° Centigrade because that's body temperature. All of our studies are made at 37° Centigrade.

Now, there are two more things that should be considered and they are: What was the cause of the thrombocytopenia? Were all factors ruled out? Was she taking drugs, continued on drugs, or was there an infection which started it or did it just come out of the clear, blue sky? It's very informative to try to find the causative factors. Often we can't and probably in this case that was true.

The other is a very important question. How long should we stay with conservative treatment before we resort to splenectomy? There was a time when a patient had a low platelet count and by the next morning the spleen was out. Dameshek did a good job when he put the fear of God into us regarding splenectomy. Perhaps it isn't as dire as Dameshek says, but nevertheless he has accomplished a great deal of good in showing that we should be conservative, especially in children, regarding splenectomy, because most children recover spontaneously even though sometimes it takes months before they do. Now in this case where the dose of prednisolone had to be so big, probably a splenectomy was very definitely indicated and the results were very favorable. In an adult it's somewhat different than it is in children. These are the only comments that I have to make on this particular case.

#### Dr. Angle

Thank you, Dr. Quick. Dr. Kenney, do you have any comments on this case?

#### Dr. Bergere A. Kenney

The question of drugs and other causative factors had all been gone into and there was no evidence of any inciting cause.

#### Dr. Charles Beeson

Should anticoagulants be used in postoperative care after splenectomy?

#### Dr. Quick

We haven't used them and so far we've gotten

along well. I am inclined not to use anticoagulants but to use other methods, like leg exercises, deep breathing and the full gamut of measures to prevent postoperative thrombosis. Of course, we haven't done many splenectomies. We've been very conservative in Milwaukee.

#### Dr. Chris L. Mengis

I just wanted to know, out of curiosity, if a Coomb's test was done?

#### Dr. Angle

Yes it was, and it was negative.

#### Dr. Angle

Case #2. A.P.

This white female patient, aged 32, a gravida VIII, and a para V, with two previous stillbirths, entered the hospital in active labor and during the second stage of a normal delivery, became nauseated and cyanotic with stertorous respirations. A limp infant was delivered which could not be resuscitated.

After repair of a second degree perineal tear, the patient went into severe shock with no pulse or blood pressure and with moderate vaginal bleeding. Rales were detected in the left lower lobe posteriorly and an electrocardiogram showed a deep S-1 and depressed RST-2, AVL, and V-1-6. A chest x-ray showed only elevation of the dome of the left diaphragm. Fibrinogen level was reported as 184 mg./100 ml. of blood although there was no evidence of clotting of the vaginal blood.

The patient was given six grams of human fibrinogen intravenuously and 2,500 ml, of whole blood with complete correction of shock. Her subsequent course was stormy, featured by renal failure, staphylococcal enteritis, enteritis and urinary infection due to C. albicans and evidence at present of postpartum necrosis of the pituitary with diabetes insipidus.

#### Dr. Quick

Of course, in the back of my mind is this question: Is this a true representative of the acquired afibrinogenemia? The fly in the ointment is this first fibrinogen determination. It would be much easier to discuss this case if we didn't have this

fibrinogen determination staring at us because 184 mg./100 cc. is not normal, but certainly a fairly good level of fibrinogen. I am inclined to believe that probably it could have been taken after a transfusion had been given.

#### Dr. Angle

No. It was taken prior to transfusion.

#### Dr. Quick

I think it's a little difficult to discuss this because we do not have complete evidence of the so-called postpartum afibrinogenemia. Of course, you know that this condition is one of the relatively common conditions in obstetrical bleeding. There are three causative factors: a dead fetus which has been retained for a considerable period of time; premature separation of the placenta; and, thirdly, amniotic fluid embolism. How the amniotic fluid gets into the blood stream is not known. It is quite strongly thromboplastic and can result in a whole series of conditions such as you described.

Now, we can simulate this defibringenation experimentally. We've worked several summers on this problem, injecting thrombin into dogs at a very slow rate, and we succeeded in getting the fibrinogen very low. In addition, we depleted factor V and factor VIII. Factor VII and factor IX all remained pretty normal, even the prothrombin. This, I think, has a definite bearing when we are dealing with an obstetrical problem, namely, that it isn't fibrinogen alone that is depleted. We're depleting other factors, particularly V and VIII. Therefore, I am inclined to believe, (and I'm standing pretty much alone, although there are others who voice a similar opinion), that probably the fibringen is effective therapeutically because it is impure fibrinogen and if you use very pure fibringen the results would be less favorable.

As a matter of fact, in this particular case you gave 2,500 ml. of whole blood in addition to fibrinogen. In a few cases that I have seen I have advised giving fresh frozen plasma in order to supply some of the other factors. In studying such a case, I think one approach would be to do a prothrombin time. Of course if there is no fibrinogen, you get infinity for a prothrombin time. If you mix plasma of the patient with deprothrombinized or adsorbed rabbit plasma, factor V will not be measured, but you will get some measure

of fibrinogen. You will get some prothrombin time because the rabbit plasma contains fibrinogen.

An effort should be made, I think, in cases of this type, to study other clotting factors. Of course I realize that these are emergency cases and you can't set up an array of tests unless your laboratory is well equipped. I think the handling of this case by giving fibrinogen and whole blood certainly helped this patient, but apparently a great deal of harm was done before therapy was started.

#### Dr. Angle

I would like to ask Dr. Quick one question. In some of the obstetrical literature on this problem, in attempting to account for bleeding in the presence of an above-critical level of fibrinogen, as in this case, certain investigators postulated the presence of a circulating anticoagulant which has been found only irregularly. One investigator also postulated the presence of a state of heparin-like total inhibition of coagulation. Do you have any comments on that, Dr. Quick?

#### Dr. Quick

Unfortunately these cases come up when you least expect them. I have to rely mostly on the work of others because I have had very little opportunity to study this type of case. I think that the presence of heparin is not very likely. There again it doesn't take a great deal of effort to rule out heparin. There is another complication that you have mentioned, and that is fibrolysin. It has been claimed that some of this bleeding is due to liberation or activation of plasmin and that we get very active fibrolysin. There is no great agreement among workers and I am inclined to believe that the main cause of bleeding is depletion of factors V and VIII.

In the studies in which we did defibrinogenation with thrombin, after two hours the dogs developed a very pronounced bleeding state, the very opposite of what one would expect. Of course thrombin has to be given very slowly, otherwise one gets massive intravascular clotting. The body apparently can take care of the fibrin as it is formed quite readily, but we get a depletion of the other clotting factors, and I think that this probably accounts for the bleeding, in addition to the fibrinogen depletion which is actually minor in many ways. Patients with hereditary afibrinogenemia are mild bleeders.

#### Case #3: C.N.

This white female, aged 42, entered the hospital on 10.8.58, because of a twisted ovarian cyst which was removed several hours later without incident. Two hours after return from surgery there was a marked drop in blood pressure which was sustained over a two hour period during which severe shock prevailed. The abdomen became somewhat distended and doughy in consistency. Whole blood transfusions were given and the patient was returned to the operating room, at which time her abdomen was found to be full of blood. No specific bleeding lesions were found and there was no evidence of any arterial escape. The patient was noted to bleed freely from all cut surfaces.

Freshly drawn whole blood was given during surgery and all bleeding ceased. Blood was evacuated from the abdomen and the patient returned to her room with no evidence of active bleeding. Her postoperative course was thereafter normal and available coagulation studies were performed two days postoperative and three months after convalescence, with completely normal results.

#### Dr. Quick

The type of bleeding presented by Case 3 is puzzling. I am inclined to regard it as vascular caused perhaps by the lack of some agent required for normal vascular function. Stored blood fails to correct the hemostatic defect and may even worsen it, because it may bring about a certain degree of hemolysis. As a result, the clotting factor in erythrocytes is liberated which, in turn, causes comsumption of various clotting agents, thereby further decreasing hemostatic efficiency. This is speculation, but on this basis, we avoid giving large quantities of stored blood without also giving in addition fresh frozen plasma.

#### Dr. Angle

Have you any idea why it starts in the first place?

#### Dr. Quick

No. Of course there are certain possibilities that have to be considered. Could a twisted ovarian cyst lead to a depletion of platelets? Certain conditions can lead to consumption of platelets producing a picture of the type of bleeding seen in thrombocytopenia. This type of bleeding has not been studied adequately. Usually, the case presents an emergency situation and blood transfusions are started before an adequate study of the blood has been made. Furthermore, the usual routine clotting tests are not adequate.

#### A Physician

I wonder if you could mention any time after which you ought not to depend so much on plasma.

#### Dr. Quick

Frozen plasma is satisfactory for several weeks. In Milwaukee, the blood bank has a big turnover so there is no problem as to the effect of long storage.

#### Dr. Angle

#### Case #4: D.S.

This white female patient, aged 31, was admitted on 2.16.62, with sudden onset of pain in the right chest and shoulder with slightly bloody sputum. She had been in good health since the birth of her third child four months previously.

Physical examination revealed rales in the posterior portion of the right lung where the x-rays showed a question of a slight increased density, which became more localized over a period of days, with ultimate cavitation. On the day after admission, the right thigh was found to be one inch larger in circumference than the left and a diagnosis of thrombophlebitis was made. The patient was placed on Tromexan and required 1,200 to 1,500 mg. daily to maintain the prothrombin time between 24 and 30 seconds. She was discharged on 3.11.62 on a maintenance dose of 900 mg. of Tromexan daily.

On 3.19.62 the patient vomited coffeeground material and became markedly pale. On admission the prothrombin time was found to be four minutes and 30 seconds, with a control of 12 seconds. Her packed cell volume was 30 per cent, hemoglobin 10.1 grams.

Dr. Landmann, would you want to make any comment about the case itself?

#### Dr. H. Richard Landmann

The only thing about the case that disturbed me was the fact that she needed a rather large amount of Tromexan to maintain her therapeutic range, for which I have no explanation and I wonder whether Dr. Quick would comment on this. She received Tromexan for a period of three weeks, and daily we had to give her between 1.200 and 1,500 mg., so I felt fairly safe after she had clinically improved to let her go on a maintenance dose of 900 mg.

Now, whether there is any deterioration in the drug itself, if it has been stored for any length of time, I don't know. The only thing I can say is that we used the drug we had available in the hospital, but I gave the patient a prescription which she bought at a drugstore. Whether that was the difference I don't know, but as you all know, the usual maintenance dose of Tromexan is between 150-450 mg. Why this patient required so much, I don't know.

#### Dr. Quick

I think she was entitled to bleed with a prothrombin time of four minutes and 30 seconds. In the chart that I presented, Dicumarol is regarded as a vitamin K antagonist. Enough Dicumarol or Tromexan or whatever drug you use is given to counteract vitamin K, to get K out of the complex and replace it with the anticoagulant drug. In a group of patients, nearly all will respond about the same to a given dosage, but you will find that there are exceptions and I don't think any study has been made in which these exceptions have been adequately explained.

I have followed a woman with rheumatic heart disease, taking 25 mg. of coumadin daily, which is a pretty big dose, and she was getting along surprisingly well and maintaining a fairly good prothrombin level, whereas another individual taking coumadin, has been maintained for two years on five mg daily. Note the difference; one is getting five times as much as the other. I don't know why the difference. Theoretically, it's either in the rate of absorption, the rate of elimination, the rate of detoxification, or the amount of vitamin K stored.

There are so many factors that come into play. Of course, there are superimposed conditions, one of which is infection. The patient with an infection is likely to need a change in his maintenance

dose. If a patient goes on spinach feedings, he may absorb enough vitamin K to cause a disturbance and necessitate an increase in the anticoagulant drug. On the other hand, it may well have been that when your patient was given a bigger dose she wasn't absorbing all of it. There are so many different factors that it's difficult to say.

#### Dr. Fred Hanold

If you choose to use heparin and then switch over to one of the coumadin drugs, how long would you continue the heparin after starting the coumadin? There seems to be a belief that there is a rebound phenomenon which may occur.

#### Dr. Quick

Of course the prothrombin time is inaccurate when heparin is in the blood. Therefore, if you belong to the school that believes in starting the patient with heparin, the best thing is to give heparin and start the Dicumarol after a few days. Then, judging by how much the prothrombin time is increasing, taper off your heparin.

If you give heparin every four hours intravenously, blood drawn at the end of this period will be pretty well cleared of heparin and the prothrombin time will be fairly reliable. I don't know whether I've made myself clear, but I would start giving a regular dose of Dicumarol and then taper off the heparin when the Dicumarol starts to take effect, say in 48 hours. To get a fairly reliable prothrombin time, do it four or five hours after the last injection.

#### Dr. Angle

#### Case #5: M.S.

This white female patient, aged 27, was admitted to the hospital 3.31.62, for D and C for evaluation of intermenstrual bleeding. A mild adenomatous hyperplasia of the endometrium was found, bleeding stopped as expected and the patient was discharged on 4.1.62, with no evidence of active bleeding. Early on the morning of 4.5.62, the patient experienced the onset of rather severe vaginal bleeding which persisted until her hospitalization 12 hours later.

On admission, the packed cell volume was 43 per cent and hemoglobin 15 grams with a coagulation time of 12½ minutes and bleeding time of

two minutes. Vaginal bleeding was moderate with passage of clots up to eight cm. in diameter. At 5:00 p. m. repeat blood studies showed a prothrombin time of 17 seconds with a control of 12 seconds and a fibrinogen level subsequently reported as 205 mg./100 cc. of blood with prothrombin consumption of 35.5 seconds with a control of 91 seconds.

At 7:30 p. m. the blood pressure suddenly dropped to 64/40 and the pulse rose to 120 and was faint. The patient was nauseated. 50 mg. of vitamin K-1 were given intravenously, along with two grams of human fibrinogen. Evidence of free bleeding seemed to diminish and the patient was given 1,000 cc. of freshly drawn whole blood. Bleeding became very scant and her blood pressure rose to normal levels.

On the following day her prothrombin time was 17 seconds with a control of 12 seconds, partial thromboplastin time was 105 seconds with a control of 91 seconds, fibrinogen was 255 mg./100 cc. and prothrombin consumption was 45 seconds with a control of 81 seconds. The packed cell volume was 45 per cent and hemoglobin 15.2 grams, and the patient had slight vaginal bleeding. On 4.9.62 prothrombin time was 13 seconds, prothrombin consumption, 62 seconds, partial thromboplastin time 111 seconds, and there was a platelet count of 520,000 per cu. mm. with normal clot retraction.

On 4.11.62 the prothrombin time was 17 seconds, with a prothrombin consumption of 41 seconds against a control of 68 seconds.

On 4.13.62 when arrangements had been made to determine what factors would be required to produce correction of the prothrombin time, her level was found to be 13 seconds, with a control of 12, all bleeding had ceased and the patient was discharged from the hospital.

On 4.26.62 she had a slight laceration of the finger with unusual oozing of blood and her prothrombin time was found to be 16 seconds.

The patient's only past history of significance was of repeated nosebleeds as a child. At age 20 a hymenotomy was performed with vaginal examination under anesthesia, following which severe vaginal bleeding occurred and a D and C was performed which stopped all bleeding. No

coagulation studies were performed at this time. Subsequently the patient had two normal pregnancies with normal deliveries and one year prior to her last admission had a diagnostic D and C without unusual bleeding.

Her family history revealed that her mother had bled unusually following a dental extraction, following a vein ligation, and following a minor vaginal procedure. Her father had sustained one episode of bleeding from a duodenal ulcer. One sister and two of three brothers had a history of severe epistaxis as children. The patient's own two children both hemorrhaged following tonsillectomy.

#### Dr. Quick

I have seen this type of case and all the attention was directed toward the prothrombin time and the prothrombin time was probably not too significant. First of all, this prothrombin time of 17 seconds rarely causes bleeding. Furthermore, if you correct this prothrombin time with serum, you will probably find it normal (12 seconds). This represents a diminution of factor VII. Therefore, I am inclined to minimize the prothrombin studies and direct my attention to the history. First of all, she had repeated nosebleeds as a child. She had a hymenotomy and bled from that. If I remember correctly she had abnormal menstrual bleeding too.

#### Dr. Angle

It was intermenstrual bleeding, but not excessively heavy. It was not a real menorrhagia.

#### Dr. Quick

Now, there are other interesting things. Her mother bled unusually from dental extraction, following a minor vaginal procedure, and following a vein ligation. Often, when we take a history, we put in too much. The father bled from duodenal ulcer. Well, that may mean something or it may not, but the fact that the patient has one sister and two of three brothers with a history of severe epistaxis as children is significant, as is the fact that the patient's own two children both hemorrhaged following tonsillectomy. There is definitely a hereditary history of bleeding, transmitted as an autosomal dominant.

This fits in very well with von Willebrand's disease. Now, von Willebrand's disease is probably

like syphilis used to be. It simulates a lot of bleeding conditions, just like syphilis simulated a lot of diseases. It is a great masquerader. I think basically this girl has von Willebrand's disease and there are two tests I would like to see done on this patient: a tourniquet test, which very often is positive, and a bleeding time which may or may not be prolonged. Very often the nosebleeds in von Willebrand's become much less severe after adolescence. So this is rather typical and my diagnosis would be that basically this patient has von Willebrand's disease. The other findings were superimposed on the basic disease.

#### Dr. Angle

May I ask, Dr. Quick, what you would suggest in the way of treatment in this patient?

#### Dr. Quick

We have found that in von Willebrand's disease, patients respond best to fresh, frozen plasma. We have used this in the treatment of active bleeding and we have used it preoperatively, that is, we have given two units or more immediately prior to hysterectomies and various types of operations with a minimal amount of bleeding.

Again, we are dealing with something that is lacking in von Willebrand's disease which is necessary for hemostasis and so far we haven't been able to put our finger directly on it. It appears to be a factor very similar to factor VIII, but I have reason to believe that it may not be factor VIII. This is in agreement with the Swedish workers who have studied von Willebrand's quite extensively.

#### Dr. Derbyshire

I would like to make two comments. I'm not trying to be unpleasant, but I was the one who did the vein ligation and stripping on the mother and I did not think she had any hemorrhagic tendencies. I shouldn't say this, but I think it was due to a technical error in surgery and responded to a moderate amount of pressure very promptly.

Secondly, I would like to ask a question. What is the risk of fresh frozen plasma and if there is a risk, is it a calculated risk?

#### Dr. Quick

First of all, von Willebrand's is a very unpredictable disease. You can do a major operation on

a patient and have no bleeding, and later on do a tonsillectomy and he bleeds severely, or vice versa. In other words, they don't always bleed, which has misled a great many people. The bleeding time very often is markedly prolonged and then again it's normal; the disease is characterized by its inconsistencies.

The second question was about the dangers of fresh frozen plasma. I'm glad you brought that up because I think it requires definite clarification. Our fresh frozen plasma is collected from one donor. The Milwaukee Blood Center very carefully screens the donors. This pint of blood is centrifuged immediately and the plasma frozen. The chance of serum hepatitis is no greater than if you gave the patient a unit of blood.

The belief that plasma is dangerous is correct when pooled plasma is used. In the old days 20 to 25 plasmas were pooled and, of course, if one out of the 25 had hepatitis virus, the whole lot would be contaminated. By using individual donors for each unit you reduce the risk to that encountered when a pint of blood is given.

#### Dr. Robert Snow

How does the safety of fibrinogen compare with fresh frozen plasma?

#### Dr. Quick

Actually there is a great deal of danger from fibrinogen, that is, if it's collected by the Cohn fractionation, because the hepatitis virus is in that particular fraction. If you use a great number of donors and pools, you will increase that risk, so that fresh frozen plasma is much safer.

#### Dr. Angle

#### Case #6: F.S.

A 42 year old white male patient of Spanish descent was referred to the hospital in September of 1953, from another hospital in northern New Mexico. On the day before transfer the patient had been admitted to the hospital with lower abdominal swelling which was globular and which was thought to be due to a distended bladder. Catheterization failed to reveal any urine and therefore a trochar was introduced into the mass and only dark blood was obtained. He was referred to St. Vincent for further diagnosis and treatment.

On admission the patient gave a history of having had unusual bleeding in the past with hemorrhage into his knees and into his elbows, with subsequent flexion deformities of these joints. He gave a history of a brother who had died at the age of 30 of hemorrhage, and a second brother who had had episodes of hemorrhage into joints with mild deformities.

Physical examination was essentially normal except for moderate pallor and the presence of a globular swelling in the lower abdomen, with a puncture wound from which dark red blood was oozing.

Significant laboratory studies were a red blood count of 3,000,000 with 9.3 grams of hemoglobin. Differential blood count was normal and platelet count was normal. Prothrombin time was 13 seconds with a control of 13, bleeding time was four minutes and 15 seconds. Coagulation time was 36.5 and the prothrombin consumption was 20 seconds with a control of 50 seconds.

Treatment consisted of freshly drawn whole blood and intravenous Cohn Globulin Fraction 1. On this treatment the coagulation time was returned to normal, bleeding ceased and over a period of days pelvic hematoma disappeared.

#### Dr. Quick

I have very little to add to this case. When you see a patient who has ankylosis of joints you make the diagnosis almost without laboratory studies because there are very few hemorrhagic diseases that cause ankylosis of the joints. Of course everything fits, the hereditary history and so on. The only question that I cannot solve is whether this is hemophilia A or B, and that would not be very difficult to do.

#### Dr. Angle

Dr. Quick, would you comment on your recommendations for treating the hemophiliac?

#### Dr. Quick

Yes, first of all, I think that parents should be instructed as soon as the diagnosis is made to avoid chances of injury and yet there should be a balance. You can go too far so that the child is

overprotected and may develop emotional troubles. There are two very simple procedures that do a great deal of good and are often overlooked. In the hemophiliac, the application of cold and pressure can do much to control hemorrhage. I am sure that I have helped a great many hemophiliacs by that simple advice: cold and pressure.

My second advice is that they should be aware of the danger of hemorrhage after injury. If the injury is very severe, or if it is in some location where the bleeding can't be controlled, then transfusions are necessary.

There is one more important point that I would stress and that is, if a hemophiliac is in an automobile accident and sustains a head injury, cracked ribs, or internal injury of the abdomen, he be treated prophylactically with fresh frozen plasma and given several transfusions spread over the first few days after the accident. So often the bleeding in hemophilia is a delayed bleeding that occurs three or four days after the injury and appears to be due to a breakdown of tissues.

I could probably illustrate that with this case: I have been studying a family of mild hemophiliacs and getting the case histories of as many members of the family as possible and one history is particularly interesting. This man was a very mild bleeder. He was involved in an automobile accident and fractured ribs. He was taken to a hospital. Nothing was done — no reflection on the hospital, but this hasn't been fully appreciated — and he was discharged after three days. His wife called to take him home, a distance of about 40 miles, and on the way this man developed a massive hemorrhage into his chest. He was taken back to the hospital but he died that following night.

I saw another case of a more severe hemophiliac who was in an automobile accident and sustained a head injury. He felt perfectly fine and consequently no treatment was given. He was kept at home and about the fourth day there were symptoms and signs of cerebral damage. He went into a coma and died before anything could be done. At autopsy it was found he had a massive hemorrhage in his brain. This should be borne in mind, that very often, by prophylactic treatment, delayed bleeding can be avoided.

## Combined Therapy of Upper Gastrointestinal Disorders

A Four-Year Study

SAMUEL E. STUART, M.D., Dallas

Multiple drug therapy usually is justified for a pathological condition which presents many facets of cause and symptomatology. This is especially true in diseases of the upper gastrointestinal tract, where the symptoms usually and basically are founded on an excessive stimulation of the central and autonomic nervous systems.

A combination of aluminum and magnesium hydroxides has long been known to be efficacious in counteracting the gastric hyperacidity which is so much at the heart of the difficulty in gastritis and peptic ulcer; but recent ulcer therapy has more and more leaned toward the adjunctive use of anticholinergic agents. Spasm and hypermotility of the gastrointestinal tract yield readily to such agents, which depress the autonomic function without too greatly promoting the more trouble-some effects of cholinergic blockade. 1,2

The psychic factor in peptic ulcer is well known and needs no comment here. It is reasonable to suppose that if a barbiturate is added to the regimen the ensuing relaxation, both central and peripheral, will aid the other medications by allowing a more profound and longer lasting respite from overactivity to the organs involved, giving them a chance to heal. Several experiments have shown that in peptic ulcer, healing of the crater tends to follow when the gastric or intestinal lumen is given a rest from the constant assault of excess hydrochloric acid so that permanent improvement sometimes follows symptomatic improvement if this can be maintained over a sufficient period of time.<sup>1,2</sup>

#### Scope and Method of Present Study

Early clinical data often color one's picture of the results of a drug study. Preliminary enthusiasm for a new product is bound to leave its mark upon the most conscientious and objectively minded investigator; and if the subjects themselves have heard reports of the efficacy of a new treatment in which they are participating, or in which they believe they are participating, they are likely to become "super-placebo reactors" and the results of the most well-controlled, blind study rendered unreliable.

While Greiner<sup>3</sup> recently has justified the continued existence of the small clinical study and report, showing that this can contribute useful data very much in advance of those derived from a comprehensive, systematic verification by statistical proofs from a large series, nevertheless clinical impressions should be required to stand the test of time.

The following data has been collected over a period of more than four years, and represents a study of 100 patients seen in private practice. All those individuals who did not return for evaluation or who were otherwise uncooperative have been excluded. All those retained in the study have been seen often and regularly, and their individual ups and downs during and before this therapy are quite familiar to this physician. The nearly universal complaint at the beginning was epigastric burning and pain, evidencing an irritative stimulation of the gastrointestinal system. Nausea, vomiting, flatulence and abdominal distention were also very frequent, as could be expected in gastritis and peptic ulcer.

There were 54 men and 46 women in the study. Their ages ranged from less than 30 to over 80 years, but 64 per cent were in the range from 41 to 70 years; 22 per cent were 40 years of age or less, and 14 per cent were over 70 years of age.

#### Examinations

Complete physical examinations and x-rays as necessary were carried out on all patients. Duodenal ulcer was demonstrable in 12 patients, and gastric ulcer in six. Diverticuli were found in three, and cholelithiasis was seen once in the x-ray of one patient with peptic ulcer, but this was not considered a primary diagnosis. In 79 patients, a diagnosis of gastritis (nearly always of the catarrhal type) was made. These conditions gave rise to epigastric pain in 90 patients, epigastric burning in 92, nausea in 20, vomiting in 17, flatulence in 60, abdominal distention in 48, and melena in one.

For this study, the medication\* prescribed for all patients was a suspension containing aluminum hydroxide gel, milk of magnesia, ambutonium bromide and butabarbital in the following proportions: each 5-cc. supplied 2.5 mg. ambutonium bromide, 8.0 mg. butabarbital and the equivalent of ½ teaspoonful of milk of magnesia, U.S.P., in aluminum hydroxide gel, U.S.P.

Dosage was kept constant at 10 cc. (two teaspoonfuls) every four hours, which furnished each patient with a daily total of 20 mg. ambutonium bromide and 64 mg. butabarbital. Moderately restricted, bland diets were individually worked out, and patients were all advised against the use of alcohol and tobacco.

Some of the patients already were familiar with the taste and consistency of aluminum hydroxide gel preparations and had had variable responses with them; they were told that the new medication was a suspension containing some additional ingredients which had proven helpful in cases similar to theirs.

Most patients were aware of the hyperacidic nature of their difficulties and had taken various antacids in the past; they needed only to know that the new combination also contained an antacid along with several other ingredients. All were cautioned to look for the autonomic side effects and to report them when they occurred. No patient was led to expect much more symptomatic improvement than that to which he had become accustomed.

Evaluation of results was necessarily somewhat subjective, just as are the symptoms in these disorders. Whenever patients were seen, they were queried closely as to amount of improvement, periodicity of improvement, and the length of periods during which improvement was experienced. Seasonal fluctuation in ulcer symptoms was taken into account.

taken into account.

For purposes of reporting, the effect of the medication was regarded as *excellent* if the patient described a complete absence of the presenting symptomatology constantly maintaind as long as the medications were taken. *Good* control was judged to have been achieved when the symptoms were either not completely controlled or where they sometimes returned for brief intervals while on treatment, but were otherwise not in evidence. *Fair* control meant any degree less than those just described, and the *poor* designation was reserved for those instances where little if any change was noted.

#### Results

This treatment resulted in a satisfactory symptomatic remission in 74 per cent of the patients, 35 per cent of whom experienced an excellent and 39 per cent a good control of their presenting complaints. Results were judged fair in 17 per cent, and poor in nine per cent, for an unsatisfactory response rate of 26 per cent.

The degree of relief increased as therapy was extended. Thus, 22 patients reported excellent or good relief after less than one week of therapy; 35 reported comparable relief within the next three weeks; and 17 took an additional four weeks before describing this much improvement. Of the patients with peptic ulcers, eight obtained good to excellent relief in one week, eight were better in four weeks, while two required eight weeks to be greatly improved.

After symptoms had completely subsided, patients were encouraged to withdraw medications for short periods and to report the effect. Although several of those who had early relief were able to adopt this suggestion before the end of a month, many continued the therapy for several months before they were willing to try to go without the medication. Whether this indicated development of a transitory psychic dependence is not known; but it evidently was correlated with the degree of relief obtained. Those who experienced the most relief were most unwilling to suspend use of the medications, even for short periods.

The beneficial results have been maintained during the entire period of observation of these patients. Since the study ran for more than four years, the enthusiasm surrounding the use of any new product probably had little influence on the outcome.

<sup>\*</sup>Aludrox® SA, Wyeth Laboratories.

#### Side Effects

The anticipated anticholinergic activities from ambutonium bromide appeared to some extent, but they were surprisingly mild. No patient complained of blurred vision. Constipation was not a problem, probably because of the magnesium hydroxide component of the combination. Most patients noticed some dryness of the mouth, but none had this to a degree meriting reduction of dosage or administration of pilocarpine. Evidently dryness of the mouth is nearly universal when cholinergic-blocking compounds are used, and can almost be taken as an indicator that an adequate amount of the agent is being administered to depress the overstimulated autonomic nervous system.

Side effects severe enough to require discontinuation of the medication occurred in two patients. One of these developed an allergic rash after four days; when therapy was stopped, this disappeared, only to reappear when the medication was restarted for one day. Another patient reported dizziness and refused to continue. No nausea developed in any patient who had not previously had this symptom. In the entire group, there was no incidence of withdrawal symptoms after the medication was omitted.

#### Summary and Conclusions

Clinical impressions of the results from using a rational combination of agents in 100 patients suffering from inflammatory upper gastrointestinal disorders are presented. The patients, almost equally divided among men and women, ranged widely in age; 79 had gastritis, 18 had peptic ulcers, and three had diverticuli. The presenting symptoms were made the yardstick of improvement; according to the extent to which these were overcome, the therapy was rated as excellent, good, fair or poor. Physical examinations included one or more x-rays for all patients.

A suspension containing aluminum hydroxide gel, magnesium hydroxide, ambutonium bromide and butabarbital was administered in uniform dosage and resulted in a satisfactory symptomatic remission in 74 per cent, 22 patients achieving this within one week. 35 within four weeks, and 17 after eight weeks. Improvement was maintained as long as patients remained on this therapy. Side effects were mild; only two persons discontinued therapy, and neither of these because of the discomfiture of autonomic blockage.

This combination of therapeutic agents has proven to be effective in treating gastritis and peptic ulcer. Lacking a more specific medical therapy for these conditions at this time, it would seem that a wider application of some such combination of drugs should be made.

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COMMUNITY SERVICE AWARD—Dr. V. V. Anderson, Del Norte, Colo., right, immediate past president of the Colorado Medical Society, presents the A. H. Robins award for community service by a physician to Dr. Richard L. Davis, La Junta, Colo., in Colorado Springs, Sept. 17, 1962, at the state society's annual meeting.



#### The Doctor as a Creative Writer\*

EDWARD PODOLSKY, M.D., Litt. D., Brooklyn, N. Y.

The creator of the greatest of all fictional detectives, Sherlock Holmes, was a physician, Sir Arthur Conan Doyle. Although the name is Irish, and Doyle was of Irish extraction, he was a native of Scotland. He was born on May 22, 1859, in Edinburgh, and spent his childhood in that city. His father. Charles Doyle, held a minor government post, but his real interest was in art and he spent his spare time in painting.

Conan Doyle was sent to Stonyhurst, a Jesuit institution. He was a great reader and early showed a talent for writing verses. However, he was lazy in his studies and not very amenable to discipline. When he graduated from Stonyhurst at the age of 16, one of the instructors said to him: "I am going to say something which you will remember in after life; Doyle, you will never come to any good."

#### Medical School

Conan's mother was determined that he become a physician. Accordingly, he entered the medical school of Edinburgh University in 1876. He completed the courses creditably and took his degrees of Bachelor of Medicine and Master of Surgery, followed later by an M.D. While a medical student he met Dr. Joseph Bell, a leading Edinburgh surgeon. Dr. Bell was a great diagnostician. "Use your eyes," he would say to the students as they followed him through the infirmary wards or observed him at work in the outpatient department. "Use your ears, your brains, your bump of perception, and your powers of deduction." He would astonish students and patients by his ability not only to diagnose a case but to read character and occupation from the appearance of the patient and his clothing. This made a profound impression on Doyle.

Dr. Bell made Doyle his outpatient clerk and thus the admiring young student had a good opportunity to observe his instructor's methods.

After completion of his medical studies, various adventures, and a disagreeable interlude as assistant to a college friend in the practice of medicine, Doyle decided to establish himself in practice. Although he had only fifty dollars, he took a house in Southsea, the residential quarter of Portsmouth, and put out his shingle. For twenty dollars he acquired enough secondhand furniture to equip a room in which to receive patients. Except for a bed and very little kitchen equipment, the house remained unfurnished for many months. Patients were slow in coming and in his leisure hours he began to write stories, and occasionally sold one.

During his eight years in Southsea, Doyle's writing was subordinate to his medical work. His practice was never large, but it brought sufficient income to enable him to marry and live comfortably.

#### First Appearance

These years at Southsea saw the first appearance of Sherlock Holmes. Doyle always had been interested in the detective stories of Edgar Allan Poe and now thought of trying his own hand at this form of fiction. He believed that the first essential was a chief character of an original and striking type, and his old teacher, Dr. Bell, returned to his mind. Doyle was also a great admirer of the American physician-author, Oliver Wendell Holmes. Thus he chose the name of Holmes for his detective. As companion and foil to the great detective he chose a medical man. Dr. John Watson.

The pair made their first appearance in a novel, A Study in Scarlet. This manuscript was rejected by many publishers and, in desperation, Doyle sold his rights for \$125. The story later sold millions of copies in English and many other languages throughout the world.

<sup>\*</sup>This is the first part of a two-part article on 'The Doctor as a Creative Writer.' The second part will be published in the December edition of SOUTHWESTERN MEDICINE.

Doyle did not think very highly of his first novel. He was anxious to produce more serious fiction, and the historical novel particularly appealed to him. He wrote two novels of this type, Micah Clarke and The White Company, while he was practicing at Southsea. Doyle took great pains with his research and pictured with accuracy and vividness the periods of which he wrote. Both books met with a good reception from the critics, and The White Company eventually had a wide sale.

In spite of his increasing interest in literature, Doyle continued to think of medicine as his real profession and began to think that he was not getting very far at Southsea. He had become interested in diseases of the eye and felt that he would be happier if he could establish himself as an eye specialist in London. Accordingly, he gave up his home and practice in Southsea, and after a period of study in Vienna, he and his wife went to London.

"I was aware," he says, "that many of the big men do not find time to work out refractions, which in some cases of astigmatism took a long time to adjust when done by retinoscopy. I was capable in this work and liked it, so I hoped that some of it might drift my way. But to get it, it was necessary that I should live among the big men so the patient easily could be referred to me."

He took rooms close to Harley Street, where the most eminent medical men in London were established. There he waited in his consulting room and nobody waited in the waiting room. Disheartening as this was, it had its compensations. He had plenty of time to write. From this consulting room came the first short stories about Sherlock Holmes, and they immediately caught the fancy of magazine editors and readers.

In the spring of 1891, Doyle had a severe attack of influenza. As he lay in bed convalescing, he became convinced that his future lay in literature rather than medicine. He determined to give up medical practice and devote all his time to writing.

From then on Doyle was occupied solely with writing. The only medical work in which he engaged after that was as a voluntary surgeon with the British forces in South Africa during the Boer War. An outbreak of typhoid gave him a terrible

experience during his Army Service. Except for this episode, demands upon the doctors with the British Army were not heavy, and Doyle found time to observe much of the fighting. He began work on a history of the war, which he completed and published on his return to England. As a patriotic Briton he was distressed by the fact that public opinion in many countries tended to favor the Boers. He conceived the idea of writing a defense of the British position and a refutation of the charges made against the British Army in South Africa, to be published in pamphlet form and distributed free to statesmen, journalists and other makers of public opinion throughout the world. He carried out the project with great success and it was in recognition of this work that a knighthood was bestowed upon him in 1902.

#### Prolific Writer

Arthur Conan Doyle was a prolific writer. During his career he produced nine volumes of the Sherlock Holmes series, eight historical novels, 13 other volumes of fiction, a book of verse and one of literary criticism, two works on the Boer War and a history of the British campaigns in Europe during the First World War, several plays, and a number of books on spiritualism.

In spite of his heavy literary program Doyle engaged in many other activities. He was active in politics, ran twice for Parliament, but was never elected; traveled widely and produced plays, among them his own. He interested himself in various causes, including the movement for reform of the divorce laws in England and the humanitarian campaign to ameliorate the condition of the natives of the Congo under King Leopold of the Belgians.

In his later years, Doyle's time and energies were increasingly given to his advocacy of spiritualism. While in Copenhagen on a lecture tour in the fall of 1929, he was stricken with heart disease. Despite repeated severe attacks, he refused to give up his tour and went through with it to its scheduled end, sometimes giving two lectures a day.

#### Carried Ashore

When he returned to England he had to be carried ashore. He was booked to give two lectures in London two days later. Disregarding his condition and the advice of a heart specialist, he fulfilled his engagements. In his autobiography he wrote, "That was on November 10 and I write now late in February. I never have walked 100 yards outside my door between those dates." On July 7, 1930, he died at the age of 71.

One of the greatest of short story writers was Anton Chekov, who was born Jan. 17, 1860, in the old Black Sea port of Taganrog. His father, the son of a serf, had married a merchant's daughter and settled in Taganrog where he carried on an unsuccessful trade in provisions during Anton's boyhood. The family was large and its income meager, and the youthful Anton was pressed into his father's business at an early age. He worked cheerfully and, observing customers and idlers in the store, he gathered many droll stories which he was fond of whispering to his schoolmates.

#### Remarkable Progress

When Anton was about fourteen his father moved to Moscow, but the son was left behind. Now having time to devote to studies, his progress in school was remarkable. At the age of 17 he wrote a long tragedy which he later destroyed. He was graduated with honors from high school in Taganrog and while studying medicine at the University of Moscow he began to write short stories as a means of aiding his struggling family. His first published literary effort appeared in a Moscow newspaper in 1880 and was followed by many brief stories in several of the smaller publications in the city. Chekov received his M.D. in 1884 and practiced medicine for a few years, but his main interests lay in writing.

It was Anton Chekov's unceasing ambition to write a long, full-fledged novel. This was natural, since the long novel was an art which flourished in his country. He died at the age of 44 without realizing his ambition. To his dying day he had regarded his short stories, which now are regarded as masterpieces, as a kind of tuning-up preparation for the larger work to come.

Even had Chekov lived to a riper age, it is doubtful whether he would have achieved his ambition. He made several attempts to write what he called novels, but they ended in his producing rather long short stories.

Chekov had modesty, a sharp analytical mind, a passion for objectivity, and a tendency to work in harmony with the facts of science. He subjected all literary creation to this test of accuracy, objectivity, science, even of specialization. It must be remembered that he was a physician before he became a writer, and something of the physician's mood of treating cases without moral or religious bias crept into his work. Again, he rejected all that was grandiose, supernatural, romantic; he had an almost abnormal fear of "biting off more than he could chew," and this fear he tried to instill into all literary aspirants who sent him their compositions.

Chekov was a victim of his own temperament. This is not to say that his stories lacked warmth or poetry. Indeed, they had both in abundant measure. Surely, they are "slices of life"; but they do not make a whole loaf. Because of his preoccupation with science and objective accuracy, he employed the microscope in dissecting human emotions, and in this process he seems to have become fascinated by the fragment, thus possibly losing the sense of the whole. He is, essentially, a master of the fragment. In this he is a modern in the art of fiction. He is an analyst and not a synthesist; a specialist and not a general practitioner.

#### Fear of Dullness

One factor which undoubtedly hindered him from achieving a longer work was his besetting fear of dullness. A severe critic of himself, he questioned the value and interest of almost everything he wrote.

"You say," he writes in Souvorin in 1889, "that I have grown lazy. That does not mean that I now am lazier than I used to be. I work nowadays as much as I did three or five years ago. To work, and to look as though I were working constantly from nine in the morning till dinner, and after the evening meal until bedtime, has become a habit with me, and in that respect I am exactly like a government clerk—it is not my laziness that is to blame, but my inborn psychological pecularities. I do not care enough for money to make a success of medicine, and for literature I have not enough passion, and therefore not enough talent. The fire burns in me slowly and evenly, without sudden spluttering and flaring up. There is a sort of stagnation in my soul. I explain it by the stagnation in my personal life. I am not disappointed. I am not tired. I am not depressed, but simply everything has suddenly become less interesting. I must do something to rouse myself."

He also spoke of his loss of faith in letters to his friends. He "could only look with perplexity at any intellectual who does believe." We must bear in mind also his confession that "I have always tried where it was possible to be consistent with the facts of science, and where it was impossible I have preferred not to write at all."

Chekov was troubled with illness practically all his life. An obstinate cough manifested itself and Chekov went south in 1888 to a little cottage on the banks of a river where he continued to practice medicine among the villagers and peasants. The stage had always fascinated him, and the following year, although he was troubled with heart attacks, he wrote the play *Ivanoff* in two and a half weeks, and then a one act playlet, *The Swan Song. Ivanoff*, produced in Moscow, was a failure. He rewrote the play and it was put on in St. Petersburg with great success. Then fol-

lowed a farce written in a single evening, The Boor, which was a success. The next play, The Demon, was a failure, but ten years later this also was rewritten under the title of Uncle Vanya and became a great success. In 1890, Chekov made a journey by stagecoach across Siberia to the Island of Saghalien.

Tuberculosis had by now made deep inroads. He spent the last ten years of his life in the Crimea. During this time he wrote his greatest plays. The Sea Gull was produced in 1895, scoring an immediate success. The Three Sisters, produced in 1901, was also successful. His greatest play, The Cherry Orchard, was produced at the Moscow Theatre shortly before his death. He was hailed as one of Russia's greatest dramatists.

Anton Chekov, physician, author and dramatist. died in the little village of Badenweiler in the Black Forest on July 2, 1904. His body was taken to Moscow for burial, and all Russia mourned his passing.

#### N.M. Medical Society Interim Meeting November 16-17

The interim meeting of the New Mexico Medical Society will be held at Farmington, N.M., Nov. 16 and 17, 1962, with headquarters in the Town House Motel. Registration will begin at 8:00 a.m. on Friday, Nov. 16, with the first scientific session scheduled to start at 9:00 a.m.

The scientific program has been approved by the American Academy of General Practice for six hours Category II credit. Dr. John C. Mc-Culloch of Farmington is chairman of the program committee for the meeting.

The complete program follows:

#### Friday, November 16

8:00 a.m. Registration

9:00-10:00 a.m. Evaluation of Diagnostic Tests for the Diabetic State

E. Paul Sheridan, M.D.,

Denver

10:00-11:00 a.m. Oral Therapy in Diabetes Mellitus

W. R. Kirrley, M.D.

W. R. Kirtley, M.D., Indianapolis

11:00-12:00 a.m. Management of Juvenile and Labile Diabetes Mellitus E. Paul Sheridan, M.D.

#### Saturday, November 17

8:00 a.m. Registration
9:00-10:00 a.m. Acute Complications of Diabetes; Hypoglycemic Reactions and Diabetes Ketosis
W. R. Kirtley, M.D.

10:00-11:00 a.m. Management of the Pregnant and Surgical Diabetic
E. Paul Sheridan, M.D.

11:00-12:00 a.m. Various Insulins and Their Usage
W. R. Kirtley, M.D.

#### Southwestern Medicine Writing Awards Winners Named

Winners in the first annual Writing Awards Contest of *Southwestern Medicine* were announced at the 44th annual meeting of the Southwestern Medical Association in Albuquerque, October 18-20.

Judging was done by the educational committee of the American Medical Writers' Association, of which Dr. Richard H. Orr is president. The awards were established by Paul I. Murphy, president of the Medical Research Association of New York and Boston, to encourage improvement in medical journal writing. The awards, signed by Dr. Lester C. Feener, Editor of Southwestern Medicine, and Dr. Louis W. Breck, Managing Editor, were as follows for the 1961-62 year:

National classification. First place. \$100. Dr. Armand J. Quick, Department of Biochemistry at the Marquette University School of Medicine at Milwaukee, Wis., for his article on "Mechanism of Blood Coagulation" in the July, 1962, issue. Second place, \$75. Dr. Carv M. Dougherty, Clinical Associate Professor in the Department of Obstetrics and Gynecology at the Louisiana State University School of Medicine at New Orleans, for his article on "External Version in Breech Presentation" in the June, 1962, issue. Third place, \$50, Dr. Wilfred Dorfman, Brooklyn, N. Y., Department of Psychology in the Downstate Medical Center in New York, for his article on "Depression and Psychosomatic Illness" in the May. 1962, issue.

Regional classification. First place, \$100. Dr. John F. Currin and Dr. Albert Daniels, Flagstaff. Arizona, for their article on "Abdominal Pain and Shock in Hemochromatosis: A Possible Explanation" in the January, 1962. issue. Second place, \$75, Dr. M. P. Spearman, El Paso, "On the Nose", April, 1962, issue. Third place, \$50, Dr. M. R. Chappel, Tucson, Director of Student Health at the University of Arizona, "Infectious Mononucleosis", June, 1962, issue.

The Editors of Southwestern Medicine have announced that the contest will be continued for the second year, 1962-63, with judging of original

scientific articles starting with the September, 1962. issue and concluding with the August, 1963, issue.

#### More Awards Next Year

Once again the awards will be provided by Mr. Murphy in the same amounts for national and regional classifications as in the first year.

The regional classification will include physicians who practice in West Texas, Arizona, New Mexico, Nevada or Northern Mexico. Physicians in the U. S. outside the regional area may compete for the national awards.

Contributions must be written in English. They must be typed, double spaced, on one side of the paper only. All papers should be submitted to Lester C. Feener, M.D., Editor, 310 North Stanton Street, El Paso, Texas. As with all official medical journals, only those papers found acceptable by the Board of Editors of the journal will be published.

#### Coming Meetings

Southern Medical Association, annual meeting. Fontainebleau Hotel, Miami Beach, Nov. 12-15, 1962.

New Mexico Medical Society, Interim Meeting, Town House Motel, Farmington, N. M., Nov. 16-17, 1962.

University of Colorado School of Medicine, ninth annual General Practice Review, Denver, Jan. 13-19, 1963.

Arizona Academy of General Practice, third annual Seminar, "Psychiatry in the Practice of Medicine," Arizona State Hospital, Phoenix, Feb. 9-10, 1963. Address inquries to: James L. Grobe, M.D., 2610 West Bethany Home Road, Phoenix 17, Arizona.

New Mexico Chapter, AAGP, Ruidoso Summer Clinic, Ruidoso, N. M., July 15-18, 1963.

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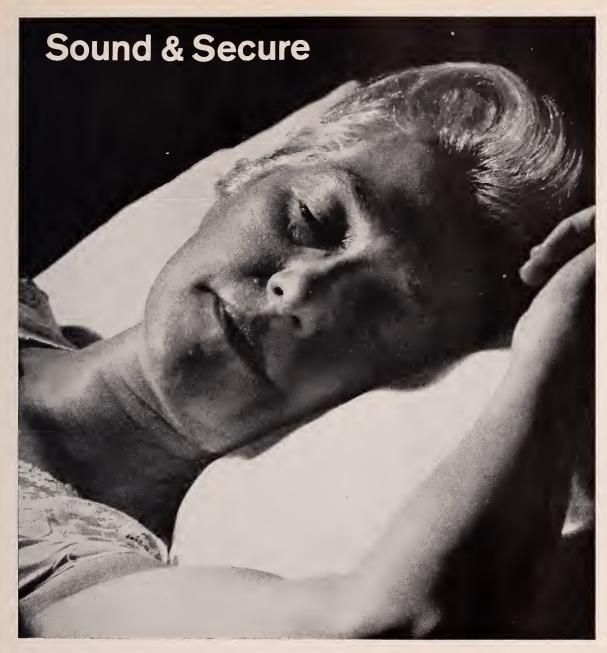
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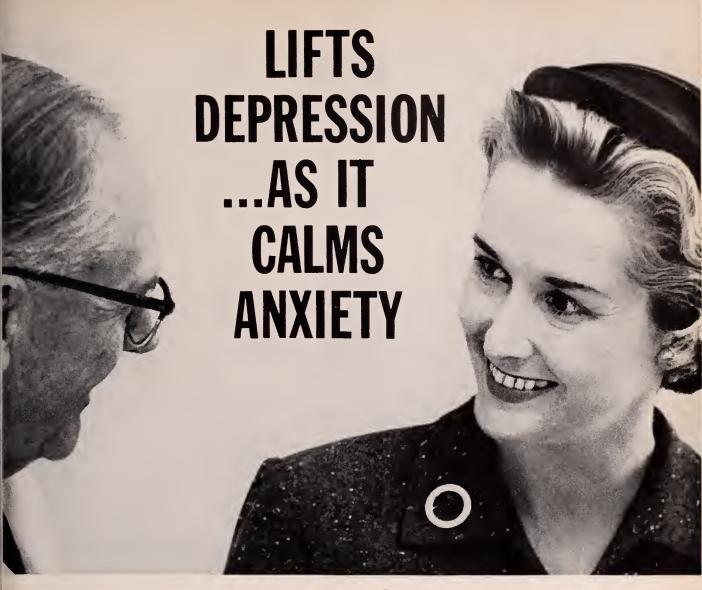
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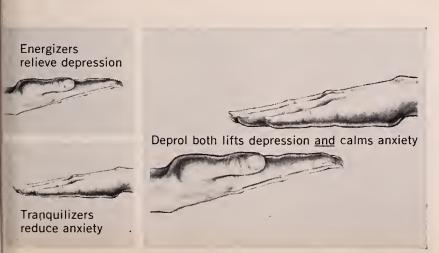
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Yoss, R. E., and Daly, D. D.: Pediatrics 25: 1025 (June) 1960

From study of 89 patients: "...the drug [Ritalin] had no effect on blood pressure, the blood count, urine or blood sugar, did not depress the appetite, and produced no tachycardia."

Natenshon, A. L.: Dis. Nerv. Syst. 17: 392 (Dec.) 1956

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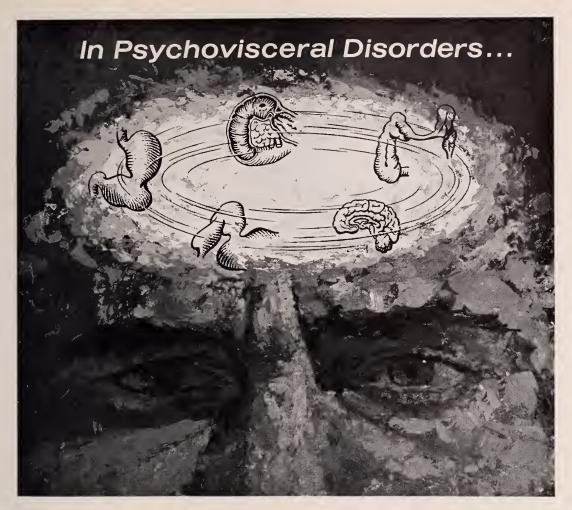
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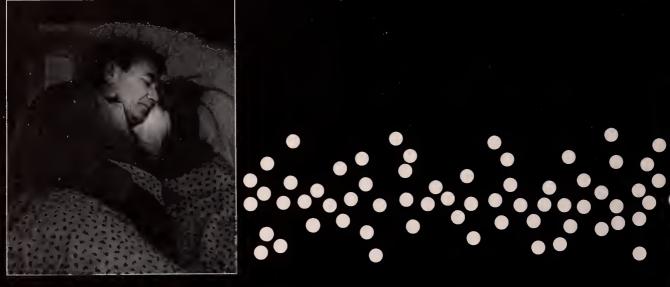
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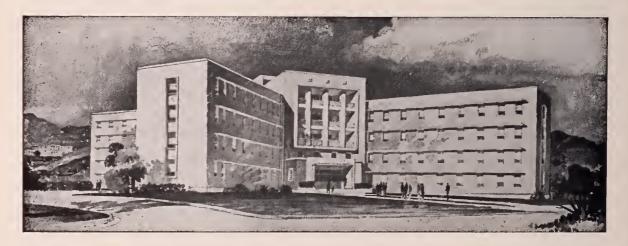
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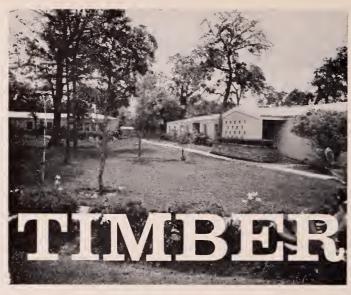
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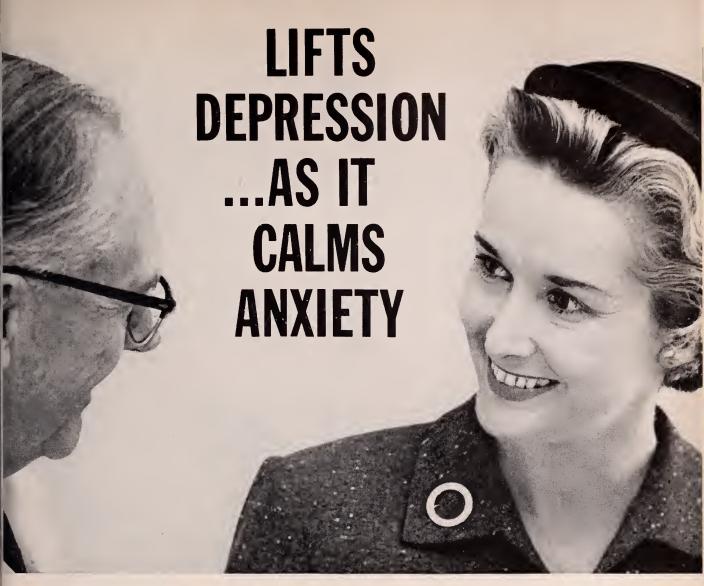
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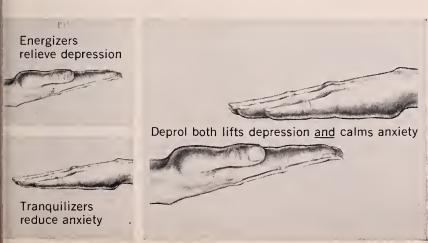
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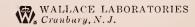
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### Santa Fe Semina

October 23, 1962, St. Vincent's Hospital, Santa Fe

### Chromosomal Abnormalities in Man

ROBERT DAY, M.D., M.P.H., PH.D. Assistant Professor of Epidemiology, University of California, Los Angeles

The discovery, in 1959, of an extra chromosome associated with clinical Down's syndrome (mongolism) opened the way for numerous studies into the relationship between chromosomal aberrations and disease. During the three years, 1959-1962, an impressive number of publications reporting new knowledge about the chromosomal abnormalities of man have appeared. With the current rapid advances in medical genetics generally and human cytogenetics specifically an understanding of the chromosomal disorders of man is an important addition to the physician's knowledge of diagnostics. This discussion attempts to outline much of the recent advance in human cytogenetics; first, by considering the nature of chromosomes and their cellular behavior, both normal and aberrant, and second, by describing the clinical findings of the frequent chromosomal abnormalities.

For many purposes the chromosomes may be considered as distinct elements of the cell nucleus with the major function of carrying the genes. Chromosomes from a wide variety of plants and animals have been studied for many years and from these investigations a generalized pattern of chromosome behavior during cell division, and of chromosome structure, has been gained. Much of this basic information has already proven applicable to man. But while knowledge about the chromosomes of many species was accumulating, studies in man were not widely performed until the decade of the 1950's. And whereas the normal number of chromosomes was traditionally held to be 48 it was not until 1956 that Tjio and Levan,<sup>2</sup> working with cultures derived from aborted human embryo lung tissue, first described the now accepted normal human chromosome number of 46.

The reason for the long acceptance of the incor-

rect human chromosome number is similar to the reason for the present burgeoning number of studies in human cytogenetics—technique. Prior to the developments in tissue culture methods and the special modifications needed for chromosome analysis, studies in man were performed on directly squashed tissues or by examination of fixed and imbedded sections. Such preparations are usually far from optimal for chromosome study. With tissue culture techniques, however, a monolayer of cells can be grown on glass, cell division stopped by colchicine treatment during metaphase, a time at which the chromosomes are contracted and thickened and most easily observed, the cells swelled by hypotonic treatment and the preparation then squashed or air-dried and ready for study.3 This culture-colchicine-hypotonic-squash or air-dry sequence can be applied to cells derived from many organs and with numerous modifications.

Currently a similar method using leukocytes from peripheral blood is a popular technique by virtue of the ease in obtaining the cells and the relatively short duration of the culture, 72 hours, as compared with the longer time needed for skin or other cell line cultures. Lastly, a technique is available using bone marrow aspirate in which the culture is omitted, only the colchicine and hypotonic procedures in the sequence are followed and a result is obtainable within two or so hours.5

As stated before the normal chromosome number in man, termed the diploid number (2n) is 46. Figure 1 represents the normal chromosomes of the human male and the array pictured, termed a karyotype, is made by cutting out and assembling the individual chromosomes from a photomicrograph of a representative nucleus. The chromosome set is composed of 23 pairs and the members of each pair are termed homologues. Structural differentiation between pairs and structural similarities within pairs is broadly possible. Pairing and grouping are accomplished first on the basis of overall length and second by the location of the

From the Department of Preventive Medicine and the School of Public Health, University of California, Los Angeles, and the Research Division, Pacific State Hospital, Pomona, California, and Sonoma State Hospital, Eldridge, California.

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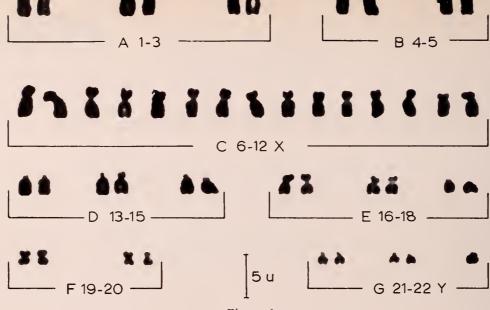


Figure 1
Karyotype of the Normal Male.

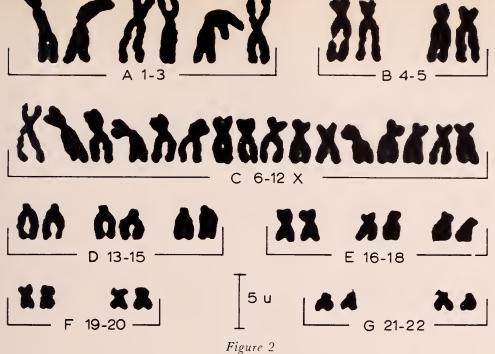
centromere, the point at which the chromosome arms converge. A ratio of the length of long to short arms can be calculated and varies from one, where the arms are of equal length, to relatively very high numbers when the short arm is very short in comparison to the length of the long arm. Due to limitations in the currently available techniques grouping of chromosomes is often followed. Thus, members of group B, identified by relatively high long to short arm ratio and by the overall length, would not be confused with members of groups A or C. Accurately pairing the true homologous chromosomes of pairs four and five, however, would be very difficult.<sup>6</sup>

This terminology can be expanded. By using the overall chromosome length and the arm ratio based on the centromere position, any chromosome can be indicated as mediocentric or median (arm ratios near one), sub-median or sub-mediocentric and, where the centromere is very nearly terminal, as acrocentric. Then the overall chromosome length relative to the other chromosomes with similar centromere position can be added in and the chromosome in question identified as, for example, a short acrocentric (group G), a long acrocentric (pair one of group A), etc. In 1959 at a meeting in Denver a convention for uniform description of the human karyotype was adopted and the system of labeling and arraying the chromosomes used in the figures of this article follows this Denver Con-

The 23 chromosome pairs may, in turn, be sub-

divided into one pair of sex chromosomes and 22 pairs of non-sex chromosomes or autosomes. On a chromosomal level the sex difference in man lies between the XY complement of sex chromosomes in the male and the XX pair of the female. Figure 2 shows the karyotype of the human female and here there are 16 chromosomes in the C group, the two X's and two members of pairs six through 12. In Figure 1, the male karyotype, the C group contains but 15 chromosomes, one X and two members each of pairs six through 12. In addition, in the male, an extra member of the G group is present, the Y chromosome, making a total of five G group chromosomes in comparison with the four short acrocentrics of group G in the female (Figure 2).

The chromosomes shown in Figures 1 and 2, derived from sonatic cells, have duplicated themselves pending the cell division, prevented here by the colchicine treatment. This duplication is needed in order that the chromosome carried genetic constitution of the two progeny cells will be that of the parental cell. The two halves are identical and both strands are termed chromatids. At cell division the centromere would divide longitudinally with an identical chromatid distributed to each of the two newly formed cells. The genetic identities of all cells beginning with the zygote or fertilized ovum is maintained through the millions of mitoses taking place during growth, development and the life of the individual.



Karyotype of the Normal Female.

Formation of gametes, the sperm and ova, the specialized function of the reproductive tract, takes place by meiosis. The mechanisms of normal and abnormal meiosis are represented diagramatically in Figure 3. Briefly, to maintain equal genetic contributions from each parent but meanwhile keeping the chromosome number of 46 constant in the new individual, meiosis operates by reducing the number of chromosomes in the gametes to one-half, 23, the haploid number (n). This reduction to one-half the chromosome number is accomplished by the two cell divisions of meiosis (I and II). The first of these divisions, meiosis I, differs from the course of mitosis in that the two homologous chromosomes of each pair come together or synapse at the midplane of the nucleus. There are thus arrayed the 23 pairs of chromosomes, a total of 46 individual members, and meiosis I proceeds with one homologue of each pair distributed to each of the two daughter cells formed. There is no division of centromeres at meiosis I. At meiosis II, on the other hand, the mechanism is similar to a mitotic division. However, only 23 chromosomes are now present and when centromere division occurs only one chromosome (chromatid) of the original pair is distributed to each of the two newly formed daughter cells. The gamete so formed has 23 chromosomes. When fertilization occurs the equal parental contributions of 23 chromosomes from each results in the newly formed individual having the normal chromosome number of 46 (n + n = 2n = 46).

The mechanism of separation of homologous chromosomes at meiosis I and, likewise, the segregation of chromatids following centromere division during meiosis II and mitosis is termed disjunction. Failure of normal disjunction or non-disjunction can result in both members of an homologous pair (or both chromatids) going to but one of the two daughter cells formed. Such an error during gamete formation will result in a chromosomally unbalanced sperm or ovum with 24 (n + 1)chromosomes and at fertilization the zygote will then have 47 chromosomes (2n + 1), or one chromosome present in triplicate (trisomy). Similarly, mitotic non-disjunction at an early division of the embryo could result in cell lines with 47 (2n+1), 45 (2n-1) or more complex chromosome numbers, the observed number depending upon the relative viability of the cell lines involved.

The essential problem involved in errors of chromosome number arises from the extra or deficient set of chromosomally carried genes present. Other types of chromosomal abnormalities also lead to effective changes in the amount of chromosomal material and, consequently, the specific gene sets involved. In translocation for instance an extra chromosome or portion of a chromosome becomes attached via appropriate breaks to another member of the chromosome set. From the clinical viewpoint, however, the syndrome produced is generally similar whether the abnormality is one of number or one of translocation.

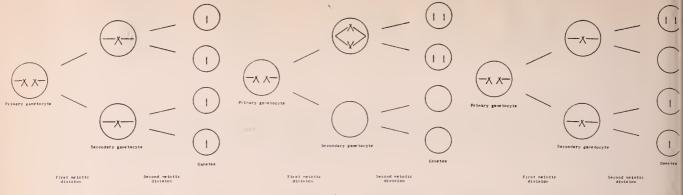


Figure 3

Meiotic Behavior, Chromosome Pair Number 21. Left, normal disjunction; center, non-disjunction at meiosis I right, non-disjunction at meiosis II.

### Clinical Aspects

Diseases resulting from chromosome abnormalities can be easily divided into those involving the sex chromosomes and those involving the autosomes.

### Autosomal Abnormalities

### Autosomai Abhormantics

1. Down's Syndrome (Mongolism, Trisomy-21). Down's syndrome is the most specific single diagnostic category occurring among the institutionalized mentally retarded, accounting for from 10-15 per cent of such patients. The incidence is fairly high; a rate of about one per 600 to one per 700 births is generally accepted. Due to the striking physical features in affected patients as well as the rather high incidence the condition has been widely studied and much was known about the disorder prior to the discovery, in 1959, of the chromosomal abberration, effective trisomy-21, consistently demonstrated in cases of Down's syndrome. Figure 4 is a representative karyotype of a male patient with Down's syndrome. Six (3-21's + 2-22's + Y) rather than the normal five (2-21)'s + 2-22's + Y) short G group acrocentrics are present. The extra chromosome is a number 21 and the probable origin is nondisjunction. A consistent and striking feature of Down's syndrome is the maternal age effect, i.e., the increasing risk of giving birth to an affected child with increase in maternal age. Reasoning from this phenomenon it is assumed that the nondisjunction occurs during oogenesis.8

The extra number 21 chromosome of Down's syndrome can also occur in translocated form. The chromosome number in patients with the translocation form of Down's syndrome is, however, 46. Here a number 21 is attached to another short acrocentric and the translocation chromosome is now in the size range of pairs 19 to 20, the F group. Or, the extra 21 combines with a mem-

ber of the D group, pairs 13 to 15, and the translocation is indistinguishable morphologically from a member of group C.<sup>10</sup> In either situation described and in the other but less frequent forms of translocation involving chromosome 21 the patient with two normal 21's plus the translocation is again effectively trisomic for chromosome 21 and has clinical Down's syndrome. The karyotype of a female with the 13-15/21 translocation form of Down's syndrome is shown in Figure 5.

An important consequence of the translocation types of Down's syndrome lies in the possible transmission in high frequency within certain families. Carriers of the translocation have been described.11, 12 Such persons have 45 chromosomes but are clinically normal. One number 21 is of the normal configuration while the other number 21 is included in the translocation. Chromosomal and genetic balance is maintained. At meiosis the translocation chromosome often pairs with the homologue of the larger translocation partner, a 13 to 15 in the case of the 13-15/21 type translocations, while the other number 21 is unpaired and presumably enters randomly into either daughter cell.<sup>13</sup> Should both the translocation (containing a number 21 gene set) and the single number 21 arrive in the gamete fertilization by a normal gamete bearing a single number 21 chromosome would result in an individual with 46 chromosomes but effectively trisomic-21. The theoretical ratios of types of gametes formed suggest that a carrier of the appropriate translocation has a one in four risk of producing either (a) another carrier, (b) an affected child, (c) a chromosomally and clinically normal individual, or (d) a zygote, presumably not viable, with but a single number 21 chromosome. The types of gametes and the offspring that may result are diagrammed in Figure 6. The risk for the translocation carrier, detected after a child

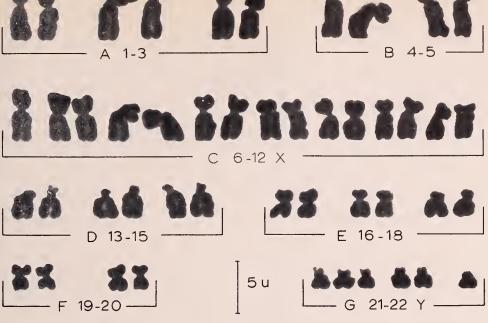


Figure 4

Karyotype of a Male with Down's Syndrome, Trisomy-21.

with Down's syndrome is born, of having another child with Down's syndrome is greatly in excess of this same chance when the first child is of the trisomy-21 type and the parental karyotypes are normal. Fortunately, the hereditary forms of Down's syndrome are quite infrequent and translocations are probably involved in under five per cent of all patients with the disorder.

Mixed cell populations, some with a trisomic-21 and others with a normal diplo-21 (2-21's) karyotypes have been reported in patients with Down's syndrome. <sup>14-17</sup> These cases are mosaics and the probable origin here is somatic non-disjunction during mitosis in the early embryo. Regardless of whether the extra 21 chromosome is present as trisomy-21, as a translocation or in a mosaic situation extra chromosome 21 material is present. Thus, chromosome study may now be considered the technique of choice in the diagnosis of Down's syndrome.

- 2. Trisomy-18. A syndrome of malformed low-set ears, hypoplastic mandible, lateral flexion deformity of the digits, probable mental and I-V septal defects and associated with the chromosome number of 47 with trisomy-18 has been described. <sup>18-21</sup> The maternal ages at birth of these patients appears elevated.<sup>22</sup> The frequency at birth is unknown but is apparently not as high as in Down's syndrome. The severe cardiac defect is usually fatal within the first six months of life.
- **3. D-Trisomy.** Several patients with 47 chromosomes and trisomy for one of the long acrocentrics

of group D, pairs 13 to 15, have been described.<sup>23</sup> A specific syndrome is involved including cleft palate and hairlip, I-V septal defect, multiple hemangiomata, mental defect, anopthalmia or other ocular abnormality and polydactyly. As in trisomy-18 these patients are severely debilitated. The life expectancy is very short.

4. Other Autosomal Abnormalities. A variety of both congenital malformations and inherited disorders have been investigated by the chromosomal technique. While most studies show negative results, an increasing number of isolated cases show a chromosome abnormality, usually not a trisomy as described for Down's syndrome and the trisomy-18 and trisomy-D syndromes, but an extra small abnormal chromosome of unknown origin.<sup>24</sup> Interpretation in these cases is often difficult. The technique of somatic chromosome analysis is as yet relatively crude. Small translocations, for example, would be undetectable as would be other structural abnormalities within the chromosome complement.

### Sex-Chromosome Abnormalities

Preceding the advances into the study of the human chromosomes was the discovery by Barr and Bertram<sup>25</sup> of the sex-chromatin body. In man and many other species a morphological sex difference in resting or interphase nuclei is detectable as a mass of darkly staining chromatin material located at the nuclear membrane and present in from 20-40 per cent of female nuclei but absent in cells of the male. The appearance of this sex-

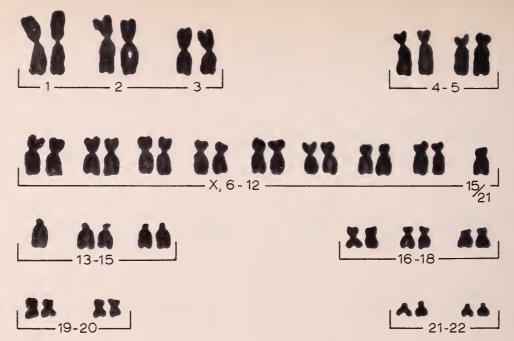


Figure 5
Karyotype of a Female with the '15/21' Translocation Form of Down's Syndrome.

chromatin body is shown in Figure 7-b in comparison with a sex-chromatin negative male nucleus of Figure 7-a. Determination of sex-chromatin is easily accomplished. Cells from most tissues are suitable; however, because of easy availability the buccal smear is the method of choice. A scraping of buccal epithelium (using a tongue blade) is smeared onto a slide, the preparation fixed immediately in Pap or other fixative and stained with one of a variety of nuclear stains.<sup>26</sup>

Study of buccal smears from patients with several forms of sex disorders indicated that contrary to expectation the male with Klinefelter's syndrome was often sex-chromatin positive while the female with Turner's syndrome was usually sexchromatin negative. Using the somatic chromosome technique it was rapidly shown that the chromatin positive Klinefelter males had an XXY sex chromosome complement, 27 with a chromosome number of 47 while the chromatin negative Turner females had 45 chromosomes and but a single X.28 Extension of the technique of nuclear sexing using the buccal smear method has uncovered a number of variants of Klinefelter's syndrome as well as females with XXX and XXXX sex chromosome complements.

Indirect assessment of the number of sex chromosomes utilizing the results of nuclear sexing follows the rule: the number of X chromosomes = the number of sex-chromatin bodies + 1. The triplo-X female has two sex-chromatin bodies in a proportion of buccal smear nuclei (Figure 7-c)

and the karyotype (Figure 8) shows a total of 47 chromosomes including three X's. As explanation for this relationship between the number of sexchromatin bodies and the number of sex chromosomes the view that all but one of the X chromosomes are out of phase with the activities of the autosomes seems most plausible.<sup>29</sup> Thus, sex chromosomes in addition to the first are detectable as sex chromatin bodies due to this difference in behavior within the cell.

The basic abnormality involved in the production of sex chromosome abnormalities is similar to that of the autosomal disorders - non-disjunction. At meiosis I of oogenesis the homologous X chromosomes pair and normal formation of ova would include a single X chromosome (chromatid) in the functional gamete. Non-disjunction, however, could result in unbalanced ova and a similar situation is possible in spermatogenesis. Here the X and Y synapse at meiosis I and the normal course of gametogenesis results in two spermatids each carrying a single X chromosome and two that are Y bearing. Non-disjunction by interfering with this normal process would result in unbalanced sperm which, when fertilizing, would in turn produce one of several sex-chromosomally abnormal embryos. More complicated sequences of non-disjunctions are possible and some in fact must be postulated in explaining the variety of sex-chromosome abnormalities observed.

Table 1 summarizes the resulting zygotes and the clinical features during life in selected instances

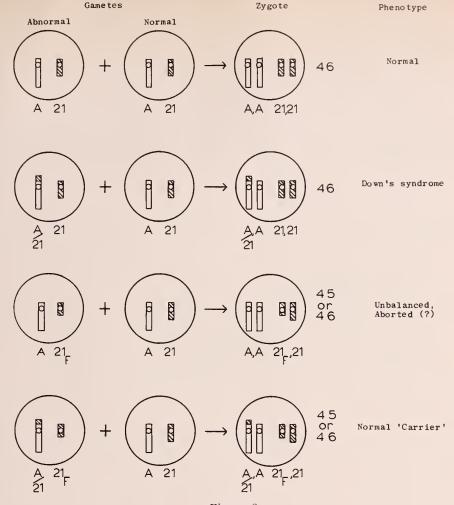


Figure 6

Expected Gametes, Zygotes and Clinical (Phenotype) and Chromosomal Types of Offspring from a Balanced Carrier of the '15/21' (A/21) Translocation Form of Down's Syndrome. 21<sub>F</sub>, fragmentary chromosome No. 21, whether present or not is of no presumed genetic importance.

of sex-chromosome abnormalities. Several of the clinical syndromes resulting from the underlying abnormalities of the sex chromosome complement are considered below.

1. Klinefelter's Syndrome. Clinically, Klinefelter's syndrome is characterized by small testes, infertility, and a high F.S.H. titer and often by gynecomastia, disproportionally long lower body segment and mental defect. Buccal smear surveys of newborn males suggest that about 2.5 per thousand live births show the basic chromosomal abnormality of Klinefelter's syndrome, 47 chromosomes with an XY sex chromosome complement.30 Many nuclear sexing studies have been done in institutions for the mentally retarded and the rate of Klinefelter's syndrome among the survey groups approaches 10 per thousand or about one per cent.31 There appears to be then a concentration of cases of Klinefelter's syndrome among the mentally defective. However, the frequency of chromatin positive (XXY) Klinefelter's syndrome among infertile males is also high; in a sample of males attending an infertility clinic a value of three per cent has been reported.<sup>32</sup>

The clinical features of Klinefelter's syndrome are very variable.33 While some patients tend towards rounded body contours with a female escutchon and reduced or absent axillary, chest, and facial hair, gynecomastia and a general feminine appearance, others are very masculine in body build. The best clinical sign for diagnosis is the finding of small testes and the presence of a positive buccal smear implying an XXY sex chromosome complement. Where mental defect is present it is usually of mild degree. Psychological problems in some mental defectives with chromatin positive Klinefelter's syndrome include abnormal sexual behavior.34 A buccal smear survey among institutionalized sex offenders with normal intellectual development revealed a higher frequency, about

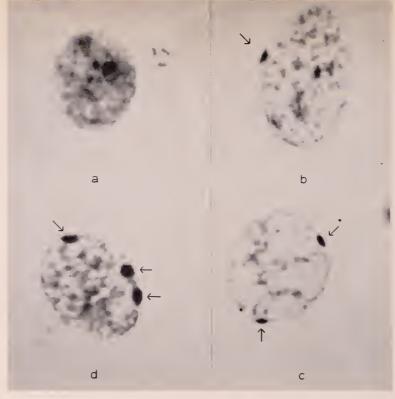


Figure 7

Sex Chromatin Bodies (Arrows) in Buccal Nuclei. (a) Normal male, sex chromatin negative. (b) Normal female, single sex chromatin body. (c) Female, triplo-X syndrome, double sex chromatin bodies. (d) Female, XXXX sex chromosome, 3 sex chromatin bodies.

one per cent, than would be expected from the frequency at birth of 0.25 per cent.<sup>35</sup>

Chromosomal variants of Klinefelter's syndrome have been described.<sup>36</sup> The few XXXY males reported do not greatly differ in clinical picture from the XXY males detected by buccal smear surveys in mental deficiency institutions. Several mosaic varieties are also known: XX/XXY, XO/XY/XXY.<sup>37</sup> A few cases of XXXXY males have been described and these patients differ from the XXY and the XXXY cases in having cleft palate, synostosis of the radial and ulnar heads, bifid scrotum and a very abnormal testicular histology.<sup>38</sup>

2. Turner's Syndrome. Patients with Turner's syndrome show predominantly failure of secondary sex development. Stature is usually short, the breasts underdeveloped with the nipples often widely spaced; primary amenorrhea is a constant finding while there is often coarctation of the aorta, webbing, of the neck, and an increased carrying angle at the elbows. The majority of these patients are sex chromatin negative. The chromosome number is 45 and the karyotype shows but one X chromosome.<sup>39, 40</sup> The incidence of Turner's syn-

drome at birth is much lower than in Klinefelter's syndrome. About one per two thousand newborn females show this disorder.<sup>35</sup> Further, mental defect is not a conspicuous feature of this syndrome. The maternal age effect noted in Down's syndrome and also observed in Klinefelter's syndrome.<sup>41</sup> is not observed in instances of Turner's syndrome.<sup>42</sup>

- 3. Triplo-X Syndrome. A number of females with two sex chromatin bodies in a proportion of buccal smear nuclei have been reported.<sup>43</sup> Many such cases have been detected in surveys of mental deficiency institutions.<sup>44</sup> There are no specific clinical findings among the triplo-X females reported. Several of the patients have had children; all of the offspring examined so far have been reported as chromosomally normal.<sup>45</sup> The incidence of triplo-X cases among female newborns approaches one per thousand,<sup>35</sup> but a frequency of 4.5 per thousand among institutionalized mental defectives suggests that the XXX sex chromosome complement is in some way involved in defects of intellectual development.
- 4. Other Sex Chromosome Abnormalities. A number of patients showing various forms of abnormal sexual development associated with a

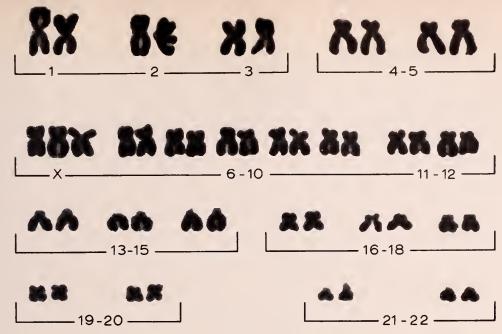


Figure 8
Karyotype of a Female with the Triplo-X Syndrome.

chromosomal aberration have been reported. In true hermaphroditism, patients with both testicular tubules and ovarian follicles, an XX in most instances and a mosaic sex chromosome complement in others have been reported.46 An abnormality of division of the X chromosome centromere, a horizontal rather than the normal longitudinal cleavage, can result in both long arms joining together to form an isochromosome. This abnormal X then carries identical genes in both arms. Morphologic recognition is possible because of a change in length away from the normal X configuration, longer when the long arms are involved and shorter than the normal X when the short arms are joined together. Patients with the isochromosome X and the normal homologue are then trisomic for whichever arm is involved in the misdivision. Similarly, patients with material missing from the X chromosome, a situation termed deletion, may show sex abnormalities. Accurate determination of the size and morphological characteristics of the sex chromatin body may be of some help in determining the presence of these deleted or isochromosome X's. In general, where the clinical problem involves improper sexual development, including primary amenorrhea and especially when associated with short stature, nuclear sexing and when indicated chromosome study are of value in the diagnostic work-up.47

Finally, mention should be made of the recently discovered chromosome abnormality in chronic granulocytic leukemia. These patients have, in a proportion of nuclei from peripheral blood preparations, an abnormal G group chromosome presumed to be a number 21 which is shorter than its normal homologue due to deletion of some material from the long arm.48 The deleted chromosome is not present in cells of origin other than blood and bone marrow, and the abnormality is thus presumed to occur after embryonic tissue differentiation has occurred. An important feature of the abnormal chromosome of chronic granulocytic leukemia lies in its specificity. Abnormalities in chromosome number and configuration are common in malignant tissues but they are not specific from case to case. The significance of the observed abnormality in chronic leukemia is not yet known. This finding does, however, hold much interest for future work.

In conclusion, the importance of maintaining a constant number of 46 chromosomes in man is emphatically demonstrated by the clinical consequences for patients with chromosome numbers other than 46. A number of specific syndromes, Down's, Trisomies-D and 18, Klinefelter's, and XXX are now attributable to the presence of a specific extra chromosome. Deviations from normal chromosome distribution during cell division (non-disjunction) provides an explanation for the presence of the extra chromosome characteristic of these clinical syndromes. Abnormalities in chromosome structure, the translocations in some instances of Down's syndrome and the deletions and isochromosomes involving the X, represent other

Normal Distribution of the Sex Chromosomes at Meiosis I: types of gametes and the resulting chromosome complements, clinical findings and number of sex-chromatin bodies (in parenthesis) in interphase nuclei.

1		SPERM				
OVA	NORMAL	NORMAL			NON-DISJUNCTION	
		CAMETES	x	Y	XY	0
		x	XX (Female, normal)	XY (Male, normal)	XXY (Male, Klinefelter's syndrome)	X/O (Female, Turner's syn- drome)
			(1)	(0)	(1)	(0)
	NON-DISJUNCTION	xx	XXX (Female, Triplo-X syndrome) (2)	XXY (Male, Klinefelter's symdrome) (1)	XXXY (Male, Klinefelter's syndrome) (2)	XX (Female, normal)
		0	X/O (Female, Turner's syndrome) (O)	Y/O (Non- viable?)	XY (Male, normal)	00 (Non-viable?)

Table I

chromosomal disorders associated with clinical disease

Indirect assessment of the number of X chromosomes by the buccal smear technique provides the physician with an additional valuable diagnostic technique in evaluating patients with abnormal sexual differentiation and development. Lastly, it may be stressed that the origin of the human chromosome abnormalities is currently beyond thera-

peutic control or prevention. However, it is of some help to parents and sometimes to patients to know that no oversight or act on their part has been responsible for the abnormality. With time and with knowledge of the complete diagnosis certainly better management of patients with a chromosomal disorder is now possible. One hopes that eventually successful therapy and/or prevention will also be available.

# A New and Ideal Estrogen for Endometriosis and for Control of Fertility

Karl John Karnaky, M.D.\*, Houston

The purpose of this paper is to discuss the dosage and advantages of a new and most potent estrogen\*\*, with minimal or almost no side effects, which causes atrophy of endometriosis in six weeks to three months instead of the usual nine months as when prescribing the progestins and micronized stilbestrol. This treatment is free of withdrawal flooding; produces a vaginal pH of 3.5

to 3.9; causes most cervical ectropions to undergo atrophy and causes fibromyomas and adenomyosis to undergo shrinking (partial atrophy).

Endometriosis is found in five to 45 per cent of the women examined at surgery. In this writer's cases, endometriosis was found in 27 per cent of those women operated for all causes.

### Therapy

(1) Endocrine therapy: Estrogenic therapy is regarded by most authorities today as the therapy of choice for endometriosis. Androgen therapy is used by some, and certainly a measure of relief

<sup>\*</sup>From the Obstetrical and Gynecological Research Foundation and Research Institute, Houston, and from the private practice of this investigator.

<sup>\*\*</sup>Nu-Estro (R) and the B-complex vitamin with Intrinsic factor-Vetatrin (R), Gateway Laboratories, Little Rock, Ark.

is obtained; but the endometriosis stops growing when androgen is given and when therapy is discontinued the endometriosis starts its mitotic activity all over again. Unfortunately, the masculinizing effects are such that continued androgen therapy is untenable.

Estrogen therapy in too small a dose and over too short a period of time is equally disappointing. This author was the first to propose massive doses of stilbestrol and estrogens for endometriosis. Since the discovery of dosage differential in estrogen therapy, many authorities, including Greenblatt, Beecham, Cooke and Haskins, have recognized its extreme value in endometriosis.

(2) B-complex with Intrinsic factor: B-complex with intrinsic factor is almost as essential to the treatment of endometriosis as are the estrogens. Estrogen and most hormones are inert without the presence of all of the B-complex vitamins. It acts efficiently in the metabolism of estrogen, but when B-complex causes complete estrogenic metabolism these B vitamins play a most important role in combating nausea caused by large doses of estrogen. It also aids in causing endometriosis to undergo atrophy.

### Effects of Massive Dosages of Estrogens

As early as 1932, Moore and Price pointed out the suppressive effects of large doses of estrogens on the release of gonadotrophins from the adenohypophysis. Many other investigators have helped delineate the complicated interrelation between ovarian estrogens and pituitary hormones.

Clinically, the sequence of events is simple. Initially, the *endometrium* becomes hyperplastic. As dosage and time increases proportionately, the endometrium becomes atrophic, or "resting". The *ovaries* also become atrophic, or "resting", with long term therapy. Over the past 17 years, this author has observed, studying more than 5000 women, that on discontinuance of massive doses of estrogen the ovaries and endometria return to normal cyclic function, as determined by endometrial biopsies, basal temperatures, and the occurrence of pregnancy.

The complete safety of truly massive dosages of estrogens has been established and confirmed by many authorities.

In not one instance has cancer been produced over the past 17 years in a large series of charity cases receiving or who had received large and prolonged doses of estrogens. Even over 10 to 15 years.

### Advantages Observed When This New Estrogen Is Being Used

During the past 17 years this investigator, who discovered estrogenic treatment for endometriosis, has treated many women with this abnormality.

- (1) Pain Relieved Almost Immdeiately: The initial observation is about patient comfort. The pain from endometriosis is relieved almost immediately, a most gratifying development both for the clinician and the patient. Pain seldom, if ever, recurs if the patient adheres to the complete dosage cycle.
- (2) Endometriosis Undergoes Atrophy Faster than with Progestine and Other Estrogen: The palpable symptoms of endometriosis disappear much sooner with therapy than with other estrogens or androgens.

This new estrogen used in this series comes in four potencies. Number 0, Number 1, Number 2, and Number 3. No patient experienced side reactions when the dose schedule was followed as given in this paper and when the estrogen was taken at 9:00 o'clock at night.

- (3) Patients are made Amenorrheic: Patients are completely amenorrheic during this course of treatment and have proven to be also anovulatory. Many patients of this group have requested to remain on reduced dosage of this new estrogen because of its complete safe inhibition of ovulation, and because side effects, for practical purposes, do not exist.
- (4) More Gratifying Results: Patients under this new therapy have an elevated sense of well being, due to the result of this conservative endocrine therapy. They have also escaped the dangerous, expensive, and debilitating surgery for endometriosis, which so often must be repeated.

With this potent new estrogen, complete atrophy of the endometrial lesions have occurred in this group of patients in six weeks to three months. No recurrences of endometriosis have been recorded in this group of case histories over the past six years.

(5) No Withdrawal Bleeding: This new estrogen has another advantage over the other

progestins and estrogens in that there is no withdrawal bleeding.

- (6) Myomas and Adenomyosis also undergo atrophy with this new estrogen which is just opposite to that of all other estrogens and progesterones used in endometriosis. This in itself is a step forward over other medications we have heretofore used.
- (7) Menstrual irregularities are usually regulated so that the endometriosis as well as the menstrual disorder is corrected.
- Vaginal pH's lowered to pH 3.5 to 3.9, a pH range in which Trichomonas vaginalis, Candida (Monilia) albicans, hemophilus vaginalis and other pathogens are destroyed.
- (9) Cervical ectropions are destroyed due to vaginal epithelial stimulation and vaginal pH.

The most effective treatment of these disorders with estrogen therapy involves the "stair step" schedule of increasingly higher doses.

First, the patient is primed with B-complex after which this new estrogen therapy is started.

During the entire course of this new estrogen therapy one to two tablets twice daily of B-complex are prescribed. As soon as the slightest amount of nausea is experienced, three B-complex tablets are taken every 1/4 to 1/2 hour until relief is obtained. It usually requires one to four doses to bring prompt relief.

After the schedule of the new estrogen therapy is completed (six weeks to three months) one to two tablets of B-complex daily is recommended to help prevent growth of the endometrial lesions. If subsequent dysmenorrhea occurs, relief is usually afforded by taking two to three B-complex tablets three to six times daily.

First week-Two of the new estrogen No. 0 tablets at night. (equivalent of 60 mg, of Estro-

Second week-Two of the new estrogen No. 1 tablets at night. (equivalent to 140 mg. of Estro-

Third week—Two of the new estrogen No. 2 tablets at night. (equivalent to 990 mg. of Estrogen.)

Fourth week—Two of the new estrogen No. 3 tablets at night. (equivalent to 1400 mg. of Estrogen.)

Thereafter—Two of the new estrogen No. 3, one to four times daily.

Note: All estrogen tablets are taken at 9:00 o'clock in the evening.

Continue at this dosage for six weeks to three months or until the endometriosis is felt to be soft and free of tenderness. Some rare patient may require four to six months of this estrogenic therapy. Patient will remain amenorrheic. Prior to cessation of therapy the dosage should be decreased gradually, reversing the four week cycle above. If excessive bleeding ever occurs while decreasing the dosage, two of the new estrogen No. 0 tablets taken every 15 minutes should bring prompt control. Oral therapy is preferred for the treatment of endometriosis; however, parenteral therapy may be used. About one-half the dosage in milligrams will suffice in parenteral therapy.

### Contraindications and Side Effects

Do not administer in the presence of malignancy. Effective control of the symptoms of functional menopausal and menstrual disorders by whatever means should rule out the continued search for pathologic etiology. No side effects have been noted other than a mild epigastric distress when taken on any empty stomach, and occasionally during a rapid increase in dosage. The administration of B-complex with Intrinsic Factor Concentrate has been found effective in preventing and/or providing relief from nausea.

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### The Doctor as a Creative Writer\*

One of the most eminent of modern living novelists. William Somerset Maugham, was trained as a physician, but early forsook medicine for literature. He was born in Paris on Jan. 25, 1874. He learned to speak French before he learned to speak English, and has always regarded France as his second home.

Maugham's happy childhood in Paris was shattered by the death of his mother from tuberculosis when he was eight years old. "Her death was a wound that fifty years have not entirely healed," he wrote in *The Summing Up*.

Two years later he lost his father and went to live with an uncle in England. The uncle was a clergyman, 50 years of age, married but childless, with fixed ideas. Maugham was not very happy in his uncle's house. When he was 13 years old he was sent to King's School in Canterbury. This new environment proved even more distasteful and he was very unhappy, chiefly because he had a severe stammer which excited ridicule among his schoolmates.

After three years a lung infection made it necessary for Maugham to leave school to spend nearly a year in the south of France, studying with a tutor. He returned to England, his health greatly improved. He returned to his old school to round out his education and then went to Germany for a year's study at Heidelberg. He now was 18 years old, and had inherited enough money from his father to provide for his education. He always felt that he wanted to write, but also thought it was wise to prepare himself for some profession. He thought that medicine best suited his tastes, and went to London to study.

His first two years of medical school did not interest him greatly, but when he began to work in the wards and as an assistant in the outpatient department, he found the work absorbing. These years proved of great value to him later as a writer. Maugham believes that not only every creative writer but also every literary critic should possess a thorough knowledge of physiology as well as psychology, "for we must know how the basic elements of literature are related to the minds and bodies of men."

While Maugham was studying medicine, he was also writing. He graduated at the age of 24,

EDWARD PODOLSKY, M.D., Litt. D., Brooklyn, N. Y. and had shown such proficiency in obstetrics that he was offered an appointment in that specialty at St. Thomas Hospital. However, Maugham refused the appointment, for at that time he had published his first novel.

This novel, *Liza of Lambeth*, was based on his work at St. Thomas. It dealt with poor people, the slums, the wretched condition under which they lived. This book was so gloomy that few people bought it and his royalties amounted only to \$100. In spite of this, Maugham determined to continue writing.

The novels that followed Liza of Lambeth fell below it artistically and it was 18 years before Maugham surpassed his first effort in this field. During that time, however, he had great success as a playwright. In 1907, one of the leading London managers presented a comedy by Maugham, called Lady Frederick. This was a great hit and other producers began to clamor for his plays. At one time Maugham had four plays running simultaneously.

His success in the theater led Maugham to devote the next few years primarily to writing plays. But there was a novel in his mind that had to be written and at last he got to work on it. The result was *Of Human Bondage*, one of the greatest novels of our time.

In painting the portrait of Philip Carey, Maugham substituted for his own stammer the more serious handicap of a clubfoot, but aside from this change the story of Philip's childhood seems to be an exact account of the author's own early years; and the same thing is true of his experiences as a medical student.

Many other novels of great distinction followed, and in a short time Maugham was established as one of the leading novelists of the day. Maugham, as a writer, has often been accused of cynicism. It is true that he has always frankly recognized the evil in the world, but he has never been blind or indifferent to the good. He accepts life as he sees it and writes of it with incompromising sincerity. His attitude is one of tolerance and compassion for the frailties of human beings. In *The Summing Up*, he reaches a fundamental conclusion about life and art which is certainly not that of the cynic. "Art," he says, "can be considered one of the great values of life only if it teaches humility, tolerance, wisdom and magnanimity."

<sup>\*</sup>This is the second part of a three-part article on "The Doctor as a Creative Writer." The third part will be published in the January edition of SOUTHWESTERN MEDICINE.





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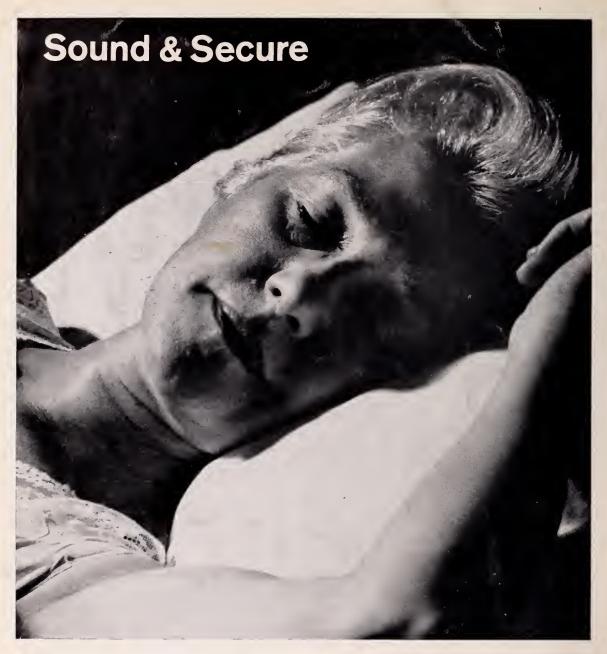
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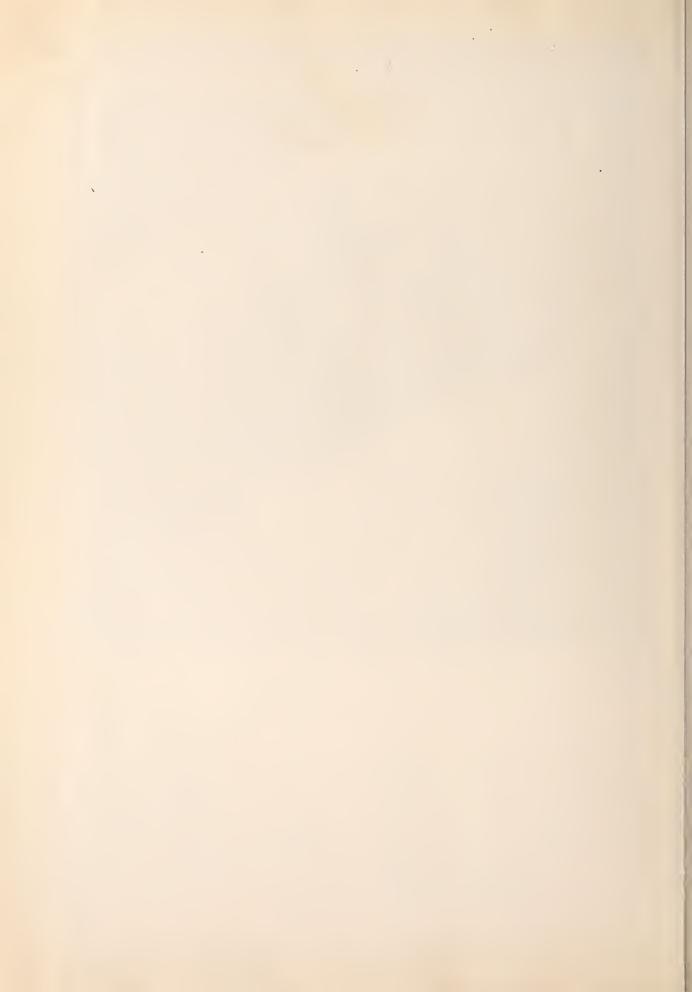
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